Form Approved. O.M.B. No. 2070-0012. Approval Expires 10-31-96.

U.S. ENVIRONMENTAL PROTECTION AGENCY

PREMANUFACTURE NOTICE

NCES

AGENCY USE ONLY

Date of receipt

Company Sanitized

Enter the total number of pages in the Premanufacture Notice ▶ 247

Sanitized Document Control Number 8T0900000188 EPA case number P-09-188

TS - M 0 3 4 A O

GENERAL INSTRUCTIONS

- You must provide all information requested in this form to the extent that it is known to or reasonably ascertainable by you. Make reasonable estimates if you do not have actual data.
- Before you complete this form, you should read the "Instructions Manual for Premanufacture Notification" (the Instructions Manual is available from the Toxic Substances Control Act (TSCA) Information Service by calling 202-554-1404, or faxing 202-554-5603).
- If a user fee has been remitted for this notice (40 CFR 700.45), indicate in the boxes above the TS-user fee identification number you have generated. Remember, your user fee ID number must also appear on your corresponding fee remittance, which is sent to EPA, HQ Accounting Operations Branch (PM-226), P.O. 360399M, Pittsburgh, PA 15251-6399, Attn. TSCA User fee.

Part I — GENERAL INFORMATION

You must provide the currently correct Chemical Abstracts (CA) Name of the new chemical substance, even if you claim the identity as confidential. You may authorize another person to submit chemical identity information for you, but your submission will not be complete and the review will not begin until EPA receives this information. A letter in support of your submission should reference your TS user fee identification number. You must submit an original and two copies of this notice including all test data. If you claimed any information as confidential, a single sanitized copy must also be submitted.

Part II — HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE

If there are several manufacture, processing, or use operations to be described in Part II, sections A and B of this notice, reproduce the sections as needed.

Part III — LIST OF ATTACHMENTS

Attach additional sheets if there is not enough space to answer a question fully. Label each continuation sheet with the corresponding section heading. In Part III, list these attachments, any test data or other data and any optional information included in the notice.

OPTIONAL INFORMATION

You may include any information that you want EPA to consider in evaluating the new substance. On page 11 of this form, space has been provided for you to described pollution prevention and recycling information you may have regarding the new substance.

So-called "binding" boxes are included throughout this form for you to indicate your willingness to be bound to certain statements you make in this section, such as use, production volume, protective equipment . . . This option is intended to reduce delays that routinely accompany the development of consent orders or Significant New Use Rules. Except in the case of exemption applications (such as TMEA, LVE, LOREX) where certain information provided in such notification is binding on the submitter when the Agency approves the exemption application, checking a binding box in this notice does not by itself prohibit the submitter from later deviating from the information (except chemical identity) reported in the form.

CONFIDENTIALITY CLAIMS

You may claim any information in this notice as confidential. To assert a claim on the form, mark (X) the confidential box next to the information that you claim as confidential. To assert a claim in an attachment, circle or bracket the information you claim as confidential. If you claim information in the notices as confidential, you must also provide a sanitized version of the notice, (including attachments). For additional instructions on claiming information as confidential, read the Instructions Manual.

☒ Mark (x) if any information in this notice is claimed as confidential.

TEST DATA AND OTHER DATA

You are required to submit all test data in your possession or control and to provide a description of all other data known to or reasonably ascertainable by you, if these data are related to the health and environmental effects on the manufacture, processing, distribution in commerce, use, or disposal of the new chemical substance. Standard literature citations may be submitted for data in the open scientific literature. Complete test data (written in English), not summaries of data, must be submitted if they do not appear in the open literature. You should clearly identify whether test data is on the substance or on an analog. Also, the chemical composition of the tested material should be characterized. Following are examples of test data and other data. Data should be submitted according to the requirements of §720.50 of the Premanufacture Notification Rule (40 CFR Part 720).

Test Data (Check Below any included in this notice)

• Environmental fate data	☐	Yes	• Other data	☒	Yes
• Health effects data	☒	Yes	Risk assessments		
• Environmental effects data	☐	Yes	Structure/activity relationships		
• Physical/Chemical Properties*	☒	Yes	Test data not in the possession or control of the submitter		

* A physical and chemical properties worksheet is located on the last page of this form.

TYPE OF NOTICE (Check Only One)

- ☒ PMN (Premanufacture Notice)
- ☐ INTERMEDIATE PMN (submitted in sequence with final product PMN)
- ☐ SNUN (Significant New Use Notice)
- ☐ TMEA (Test Marketing Exemption Application)
- ☐ LVE (Low Volume Exemption) @ 40 CFR 723.50(c)(1)
- ☐ LOREX (Low Release/Low Exposure Exemption) @ 40 CFR 723.50(c)(2)
- ☐ LVE Modification ☐ LOREX Modification

IS THIS A CONSOLIDATED PMN? ☐ Yes

# of chemicals _____
(Prenotice Communication # required, enter # on page 3)

316653

CERTIFICATION

I certify that to the best of my knowledge and belief:

1. The company named in Part I, section A, subsection 1a of this notice form intends to manufacture or import for a commercial purpose, other than in small quantities solely for research and development, the substance identified in Part I, Section B.

2. All information provided in this notice is complete and truthful as of the date of submission.

3. I am submitting with this notice all test data in my possession or control and a description of all other data known to or reasonably ascertainable by me as required by §720.50 of the Premanufacture Notification Rule.

Additional Certification Statements:

If you are submitting a PMN, Intermediate PMN, Consolidated PMN, or SNUN, check the following **user fee** certification statement that applies:

☒ The Company named in Part I, Section A has remitted the fee of $2500 specified in 40 CFR 700.45(b), or

☐ The Company named in Part I, Section A has remitted the fee of $1000 for an Intermediate PMN (defined @ 40 CFR 700.43) in accordance with 40 CFR 700.45(b), or

☐ The Company named in Part I Section A is a small business concern under 40 CFR 700.43 and has remitted a fee of $100 in accordance with 40 CFR 700.45(b).

If you are submitting a **low volume exemption (LVE)** application in accordance with 40 CFR 723.50(c)(1) or a **Low release and low exposure exemption (LoRex)** application in accordance with 40 CFR 723.50(c)(2), check the following certification statements:

☐ The manufacturer submitting this notice intends to manufacture or import the new chemical substance for commercial purposes, other than in small quantities solely for research and development, under the terms of 40 CFR 723.50.

☐ The manufacturer is familiar with the terms of this section and will comply with those terms; and

☐ The new chemical substance for which the notice is submitted meets all applicable exemption conditions.

☐ If this application is for an LVE in accordance with 40 CFR 723.50(c)(1), the manufacturer intends to commence manufacture of the exempted substance for commercial purposes within 1 year of the date of the expiration of the 30 day review period.

The accuracy of the statements you make in this notice should reflect your best prediction of the anticipated facts regarding the chemical substance described herein. Any knowing and willful misinterpretation is subject to criminal penalty pursuant to 18 USC 1001.		**Confidential**
Signature and title of Authorized Official (Original Signature Required)	Date	X
Signature of agent - (if applicable)	Date	

Part I -- GENERAL INFORMATION

Section A -- SUBMITTER IDENTIFICATION

Mark () the "Confidential" box next to any subsection you claim as confidential

Confi-dential

1a. Person Submitting Notice (in U.S.)

Name of authorized official | Position | X

Company

Mailing address (number and street)

City, State, ZIP Code

b. Agent (if applicable)

Name of authorized official | Position

Company

Mailing address (number and street)

City, State, ZIP Code | Telephone | Area Code | Number

c. If you are submitting this notice as part of a joint submission, mark (X) this box. → ☐

Joint Submitter (if applicable)

Name of authorized official | Position

Company

Mailing address (number and street)

City, State, ZIP Code | Telephone | Area Code | Number

2. Technical Contact (in U.S.)

Name of authorized official | Position | X

Company

Mailing address (number and street)

City, State, ZIP Code | Telephone | Area Code | Number

3. If you have had a prenotice communication (PC) concerning this notice and EPA assigned a PC Number to the notice, enter the number. →		Mark (X) if none →	☒
4. If you previously submitted an exemption application for the chemical substance covered by this notice, enter the exemption number assigned by EPA. If you previously submitted a PMN for this substance enter the PMN number assigned by EPA (i.e. withdrawn or incomplete). →		Mark (X) if none →	☒
5. If you have submitted a notice of Bona fide intent to manufacture or import for the chemical substance covered by this notice, enter the notice number assigned by EPA. →		Mark (X) if none →	☒

6. Type of Notice - Mark (X)

1. ☐ Manufacture Only ☐ Binding Option Mark (X)
2. ☒ Import Only ☐ Binding Option Mark (X)
3. ☐ Both

Part I -- GENERAL INFORMATION -- Continued

Section B -- CHEMICAL IDENTITY INFORMATION: You must provide a currently correct Chemical Abstracts (CA) name of the substance based on the ninth Collective Index (9CI) of CA nomenclature rules and conventions.

Mark (X) the "Confidential" box next to any item you claim as confidential

Complete either item 1 (Class 1 or 2 substances) or 2 (Polymers) as appropriate. Complete all other items.

If another person will submit chemical identity information for you (for either Item 1 or 2), mark (X) the box at the right. Identify the name, company, and address of that person in a continuation sheet. → ☐

		Confi-dential
1.	Class 1 or 2 chemical substances (for definitions of class 1 and class 2 substances, see the Instructions Manual)	
a.	Class of substance - Mark (X) 1 ☐ Class 1 or 2 ☐ Class 2	X
b.	Chemical name (Currently correct Chemical Abstracts (CA) Name that is consistent with TSCA Inventory listings for similar substances. For Class 1 substances a CA Index Name must be provided. For Class 2 substances either a CA Index Name or CA Preferred Name must be provided, which ever is appropriate based on CA 9CI nomenclature rules and conventions).	X
c.	Please identify which method you used to develop or obtain the specified chemical identity information reported in this notice: (check one). ☐ Method 1 (CAS Inventory Expert Service - a copy of the Identification report obtained from the CAS Inventory Expert Services must be submitted as an attachment to this notice) ☒ Method 2 (Other Source)	
d.	Molecular formula and CAS Registry Number (if a number already exists for the substance)	
	CAS#	X
e.	For a class 1 substance, provide a complete and correct chemical structure diagram. For a class 2 substance - (1) List the immediate precursor substances with their respective CAS Registry Numbers. (2) Describe the nature of the reaction or process. (3) Indicate the range of composition and the typical composition (where appropriate). (4) Provide a correct representative or partial chemical structure diagram, as complete as can be known, if one can be reasonably ascertained.	X

☒ Mark (X) this box if you attach a continuation sheet. Attachment 2.

Part I -- GENERAL INFORMATION -- Continued

Section B -- CHEMICAL IDENTITY INFORMATION -- Continued

2. Polymers (For a definition of polymer, see the Instructions Manual.)

Confi-dential

a. Indicate the number-average weight of the lowest molecular weight composition of the polymer you intend to manufacture. Indicate maximum weight percent of low molecular weight species (not including residual monomers, reactants, or solvents) below 500 and below 1,000 absolute molecular weight of that composition.

Describe the methods of measurement or the basis for your estimates: GPC ☐ Other ☐: (Specify) _____

i) lowest number average molecular weight: _____

ii) maximum weight % below 500 molecular weight: _____

iii) maximum weight % below 1000 molecular weight: _____

☐ Mark (X) this box if you attach a continuation sheet.

b. You must make separate confidentiality claims for monomer or other reactant identity, composition information, and residual information. Mark (X) the "Confidential" box next to any item you claim as confidential

(1) - Provide the specific chemical name and CAS Registry Number (if a number exists) of each monomer or other reactant used in the manufacture of the polymer.
(2) - Mark (X) this column if entry in column (1) is confidential.
(3) - Indicate the typical weight percent of each monomer or other reactant in the polymer.
(4) - Mark (X) the identity column if you want a monomer or other reactant used at two weight percent or less to be listed as part of the polymer description on the TSCA Chemical Substance Inventory.
(5) - Mark (X) this column if entries in columns (3) and (4) are confidential.
(6) - Indicate the maximum weight percent of each monomer or other reactant that may be present as a residual in the polymer as manufactured for commercial purposes.
(7) - Mark (X) this column if entry in column (6) is confidential.

Monomer or other reactant and CAS Registry Number (1)	Confi-dential (2)	Typical composition (3)	Identity Mark (X) (4)	Confi-dential (5)	Maximum residual (6)	Confi-dential (7)
		%			%	
		%			%	
		%			%	
		%			%	
		%			%	
		%			%	
		%			%	

☐ Mark (X) this box if you attach a continuation sheet.

c. Please identify which method you used to develop or obtain the specified chemical identity information reported in this notice (check one).

☐ Method 1 (CAS Inventory Expert Service - a copy of the identification report obtained from CAS Inventory Expert Service must be submitted as as attachment to this notice)

☐ Method 2 (other source)

d. The currently correct Chemical Abstracts (CA) name for the polymer that is consistent with TSCA Inventory listings for similar polymers.

e. Provide a correct representative or partial chemical structure diagram, as complete as can be known, if one can be reasonably ascertained.

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☐ Mark (X) this box if you attach a continuation sheet.

Part I -- GENERAL INFORMATION -- Continued

Section B -- CHEMICAL IDENTITY INFORMATION -- Continued

3. Impurities

(a) - Identify each impurity that may be reasonably anticipated to be present in the chemical substance as manufactured for commercial purpose. Provide the CAS Registry Number if available. If there are unidentified impurities, enter "unidentified."

(b) - Estimate the maximum weight % of each impurity. If there are unidentified impurities, estimate their total weight %.

Impurity and CAS Registry Number (a)	Maximum percent (b)	Confi-dential
	%	
	%	
	%	
	%	
	%	
	%	
	%	

☐ Mark (X) this box if you attach a continuation sheet.

4. Synonyms - Enter any chemical synonyms for the new chemical identified in subsection 1 or 2.

Confi-dential: X

☐ Mark (X) this box if you attach a continuation sheet.

5. Trade identification - List trade names for the new chemical substance identified in subsection 1 or 2.

Confi-dential: X

☐ Mark (X) this box if you attach a continuation sheet.

6. Generic chemical name - If you claim chemical identify as confidential, you must provide a generic name for your substance that reveals the specific chemical identity of the new chemical substance to the maximum extent possible. Refer to the TSCA Chemical Substance Inventory, 1985 Edition, Appendix B for guidance on developing generic names.

Carbon nanomaterial

☐ Mark (X) this box if you attach a continuation sheet.

7. Byproducts - Describe any byproducts resulting from the manufacture, processing, use, or disposal of the new chemical substance. Provide the CAS Registry Number if available.

Byproduct (1)	CAS Registry Number (2)	Confi-dential
None known		

☐ Mark (X) this box if you attach a continuation sheet.

Part I -- GENERAL INFORMATION -- Continued

Section C -- PRODUCTION, IMPORT, AND USE INFORMATION:

Mark (X) the "Confidential" box next to any item you claim as confidential.

1. Production volume -- Estimate the **maximum** production volume during the first 12 months of production. Also estimate the maximum production volume for any consecutive 12-month period during the first three years of production. Estimates should be on 100% new chemical substance basis. For a Low Volume Exemption application, if you choose to have your notice reviewed at a lower production volume than 10,000 kg/yr, specify the volume and mark (x) in the binding box. If granted, you are bound to this volume

Maximum first 12-month production (kg/yr) (100% new chemical substance basis)	Maximum 12-month production (kg/yr) (100% new chemical substance basis)	Confi-dential	Binding Option Mark (x)
		X	

2. Use Information -- You must make separate confidentiality claims for the description of the category of use, the percent of production volume devoted to each category, the formulation of the new substance, and other use information. Mark (X) the "Confidential" Box next to any item you claim as confidential.

a. (1) -- Describe each intended category of use of the new chemical substance by function and application..
(2) -- Mark (X) this column if entry column (1) is confidential business information (CBI).
(3) -- Indicate your willingness to have the information provided in column (1) binding.
(4) -- Estimate the percent of total production for the first three years devoted to each category of use.
(5) -- Mark (X) this column if entry in column (4) is confidential business information (CBI).
(6) -- Estimate the percent of the new substance as formulated in mixtures, suspensions, emulsions, solutions, or gels as manufactured for commercial purposes at sites under your control associated with each category of use.
(7) -- Mark (X) this column if entry in column (6) is confidential business information (CBI).
(8) -- Indicate % of product volume expected for the listed "use" sectors. Mark more than one box if appropriate. Mark (X) to indicate your willingness to have the use type provided in (8) binding.
(9) -- Mark (X) this column if entry(ies) in column (8) is (are) confidential business information (CBI).

Category of use (1) (by function and application i.e. a dispersive dye for finishing polyester fibers)	CBI (2)	Binding Option Mark (x) (3)	Production % (4)	CBI (5)	% in Formulation (6)	CBI (7)	% of substance expected per use (8) Site-limited	Consumer*	Industrial	Commercial	Binding Option	CBI (9)
	X		%	X	%	X						X
	X		%	X	%	X						X
	X		%	X	%	X						X
	X		%	X	%	X						X
			%		%							
			%		%							

* If you have identified a "consumer" use, please provide on a continuation sheet a detailed description of the use(s) of this chemical substance in consumer products. In addition include estimates of the concentration of the new chemical substance as expected in consumer products and describe the chemical reactions by which this substance loses its identity in the consumer product.

☐ Mark (X) this box if you attach a continuation sheet.

b. Generic use description — If you claim any category of use description in subsection 2a as confidential, enter a generic description of that category. Read the Instructions Manual for examples of generic use descriptions.

Component of paints, coatings, and industrial composites

☐ Mark (X) this box if you attach a continuation sheet.

3. Hazard Information -- Include in the notice a copy of reasonable facsimile of any hazard warning statement, label, material safety data sheet, or other information which will be provided to any person who is reasonably likely to be exposed to this substance regarding protective equipment or practices for the safe handing, transport, use, or disposal of the new substance. List in part III hazard information you include.

Binding Option Mark (x)

☒ Mark (X) this box if you attach hazard information. Attachment 3.

Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE

Section A -- INDUSTRIAL SITES CONTROLLED BY THE SUBMITTER

Mark (X) the "Confidential" box next to any item you claim as confidential

Complete section A for each type of manufacture, processing, or use operation involving the new chemical substance at industrial sites you control. Importers do not have to complete this section for operations outside the U.S.; however, you may still have reporting requirements if there are further industrial processing or use operations after import. You must describe these operations. See instructions manual

1. Operation description a. Identity -- Enter the identity of the site at which the operation will occur.	Confi-dential
Name	X
Site address (number and street)	
City, County, State, ZIP code	
If the same operation will occur at more than one site, enter the number of sites. Identify the additional sites on a continuation sheet, and if any of the sites have significantly different production rates or operations, include all the information requested in this section for those sites as attachments. →	
☐ Mark (X) this box if you attach a continuation sheet.	
b. Type -- Mark (X) ☐ Manufacturing ☐ Processing ☐ Use	
c. Amount and Duration -- Complete 1 or 2 as appropriate	

	Maximum kg/batch (100% new chemical substance)	Hours/batch	Batches/year
1. Batch			
2. Continuous			

d. Process description ☐ Mark (X) to indicate your willingness to have your process description binding.

(1) Diagram the major unit operation steps and chemical conversions. Include interim storage and transport containers (specify- e.g. 5 gallon pails, 55 gallon drum, rail car, tank truck, etc.).

(2) Provide the identity, the approximate weight (by kg/day or kg/batch on a 100% new chemical substance basis), and entry point of all starting materials and feedstocks (including reactants, solvents, catalysts, etc.), and of all products, recycle streams, and wastes. Include cleaning chemicals (note frequency if not used daily or per batch.).

(3) Identify by number the points of release, including small or intermittent releases, to the environment of the new chemical substance.

☒ Mark (X) this box if you attach a continuation sheet. Attachment 4.

Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE -- Continued

Section A -- INDUSTRIAL SITES CONTROLLED BY THE SUBMITTER – Continued

2. **Occupational Exposure** -- You must make separate confidentiality claims for the description of worker activity, physical form of the new chemical substance, number of works exposed, and duration of activity. Mark (X) the "Confidential" box next to any item you claim as confidential.
   (1) -- Describe the activities (i.e. bag dumping, tote filling, unloading drums, sampling, cleaning, etc.) in which workers may be exposed to the substance.
   (2) -- Mark (X) this column if entry in column (1) is confidential business information (CBI).
   (3) -- Describe any protective equipment and engineering controls used to protect workers.
   (4) and (6) -- Indicate your willingness to have the information provided in column (3) or (5) binding.
   (5) -- Indicate the physical form(s) of the new chemical substance (e.g., solid: crystal, granule, powder, or dust) and % new chemical substance (if part of a mixture) at the time of exposure.
   (7) -- Mark (X) this column if entry in column (5) is confidential business information (CBI).
   (8) -- Estimate the maximum number of workers involved in each activity for all sites combined.
   (9) -- Mark (X) this column if entry in column (8) is confidential business information (CBI).
   (10) and (11) -- Estimate the maximum duration of the activity for any worker in hours per day and days per year.
   (12) -- Mark (X) this column if entries in columns (10) and (11) are confidential business information (CBI).

Worker activity (i.e., bag dumping, filling drums) (1)	CBI (2)	Protective Equipment/ Engineering Controls (3)	Binding Option Mark (x) (4)	Physical forms(s) and % new substance (5)	Binding Option Mark (x) (6)	CBI (7)	# of Workers Exposed (8)	CBI (9)	Maximum Hrs/day (10)	duration Days/yr (11)	CBI (12)
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☒ Mark (X) this box if you attach a continuation sheet. See attachment7.

3. **Environmental Release and Disposal** -- You must make separate confidentiality claims for the release number and the amount of the new chemical substance released and other release and disposal information. Mark (X) the "Confidential" box next to each item you claim as confidential.
   (1) -- Enter the number of each release point identified in the process description, part II, section A, subsection 1d(3).
   (2) -- Estimate the amount of the new substance released (a) directly to the environment or (b) into control technology (in kg/day or kg/batch).
   (3) -- Mark (X) this column if entries in columns (1) and (2) are confidential business information (CBI).
   (4) -- Identify the media (stack air, fugitive air (optional-see Instruction Manual), surface water, on-site or off-site land or incineration, POTW, or other (specify)) to which the new substance will be released from that release point.
   (5) -- a. Describe control technology, if any, and control efficiency that will be used to limit the release of the new substance to the environment. For releases disposed of on land, characterize the disposal method and state whether it is approved for disposal of RCRA hazardous waste. On a continuation sheet, for each site describe any additional disposal methods that will be used and whether the waste is subject to secondary or tertiary on-site treatment. b. Estimate the amount released to the environment after control technology (in kg/day).
   (6) -- Mark (X) this column if entries in columns (4) and (5) are confidential business information (CBI).
   (7) -- Identify the destination(s) of releases to water. Please supply NPDES (National Pollutant Discharge Elimination System) numbers for direct discharges or NPDES numbers of the POTW (Publicly Owned Treatment Works). Mark (X) if the POTW name or NPDES # is confidential business information (CBI).

Release Number (1)	Amount of new substance released (2a)	(2b)	CBI (3)	Media of release e.g. stack air (4)	Control technology and efficiency (you may wish to optionally attach efficiency data) (5a)	Binding Mark (X)	(5b)	CBI (6)

(7) Mark (X) the destination(s) of releases to water.	☐ POTW provide name(s) below: _____	CBI	☐ Navigable waterway	☐ Other - Specify	provide NPDES #	CBI

☐ Mark (X) this box if you attach a continuation sheet.

Part II-- HUMAN EXPOSURE AND ENVIRONMENTAL RELEASE -- Continued

Section B -- INDUSTRIAL SITES CONTROLLED BY OTHERS

Complete section B for typical processing or use operations involving the new chemical substance at sites you do not control. Importers do not have to complete this section for operations outside the U.S.; however, you must report any processing or use activities after import. See the Instructions Manual. *Complete a separate section B for each type of processing, or use operation involving the new chemical substance.* If the same operation is performed at more than one site describe the typical operation common to these sites. Identify additional sites on a continuation sheet.

1. Operation Description -- To claim information in this section as confidential, circle or bracket the specific information that you claim as confidential. (1) -- Diagram the major unit operation steps and chemical conversions, including interim storage and transport containers (specify - e.g. 5 gallon pails, 55 gallon drums, rail cars, tank trucks, etc). On the diagram, identify by letter and briefly describe each worker activity. (2) -- Provide the identity, the approximate weight (by kg/day or kg/batch, on an 100% new chemical substance basis), and entry point of all feedstocks (including reactants, solvents and catalysts, etc) and all products, recycle streams, and wastes. Include cleaning chemicals (note frequency if not used daily or per batch). (3) -- Identify by number the points of release, including small or intermittent releases, to the environment of the new chemical substance. (4) Please enter the # of sites (remember to identify the locations of these sites on a continuation sheet):

_____
# of sites

☒ Mark (X) this box if you attach a continuation sheet. Attachments 6 and 7

2. Worker Exposure/Environmental Release

(1) -- From the diagram above, provide the letter for each worker activity. Complete 2-8 for each worker activity described.
(2) -- Estimate the number of workers exposed for all sites combined.
(4) -- Estimate the typical duration of exposure per worker in (a) hours per day and (b) days per year.
(6) -- Describe physical form of exposure and % new chemical substance (if in mixture), and any protective equipment and engineering controls, if any, used to protect workers.
(7) -- Estimate the percent of the new substance as formulated when packaged or used as a final product.
(9) -- From the process diagram above, enter the number of each release point. Complete 9-13 for each release point identified.
(10) -- Estimate the amount of the new substance released (a) directly to the environment or (b) into control technology to the environment (in kg/day or kg/batch).
(12) -- Describe media of release i.e. stack air, fugitive air (optional-see Instructions Manual), surface water, on-site or off-site land or incineration, POTW, or other (specify) and control technology, if any, that will be used to limit the release of the new substance to the environment.
(14) -- Identify byproducts which may result from the operation.
(3), (5), (8), (11), (13) and (15) -- Mark (X) this column if any of the proceeding entries are confidential business information (CBI).

Letter of Activity (1)	# of Workers Exposed (2)	CBI (3)	Duration of Exposure (4a)	(4b)	CBI (5)	Protective Equip. / Engineering Controls/ Physical Form and % new substance (6)	% in Formulation (7)	CBI (8)	Release Number (9)	Amount of New Substance Released (10a)	(10b)	CBI (11)	Media of Release & Control Technology (12)	CBI (13)

(14) -- Byproducts: None known (15)

☒ Mark (X) this box if you attach a continuation sheet. See attachment 8.

OPTIONAL POLLUTION PREVENTION INFORMATION

To claim information in this section as confidential circle or bracket the specific information that you claim as confidential.

In this section you may provide information not reported elsewhere in this form regarding your efforts to reduce or minimize potential risks associated with activities surrounding manufacturing, processing, use and disposal of the PMN substance. Please include new information pertinent to pollution prevention, including source reduction, recycling activities and safer processes or products available due to the new chemical substance. Source reduction includes the reduction in the amount or toxicity of chemical wastes by technological modification, process and procedure modification, product reformulation, raw materials substitution, and/or inventory control. Recycling refers to the reclamation of useful chemical components from wastes that would otherwise be treated or released as air emissions or water discharges, or land disposal. Descriptions of pollution prevention, source reduction and recycling should emphasize potential risk reduction subsequent to compliance with existing regulatory requirements and can be either quantitative or qualitative. The EPA is interested in the information to assess overall net reductions in toxicity or environmental releases and exposures, not the shifting of risks to other environmental media or non-environmental areas (e.g., occupational or consumer exposure). In addition, information on the relative cost or performance characteristics of the PMN substance to potential alternatives may be provided.

All information provided in this section will be taken into consideration during the review of this substance. See Instructions Manual and Pollution Prevention Guidance manual for guidance and examples.

Describe the expected net benefits, such as (1) an overall reduction in risk to human health or the environment; (2) a reduction in the volume manufactured; (3) a reduction in the generation of waste materials through recycling, source reduction or other means; (4) a reduction in potential toxicity or human exposure and/or environmental release; (5) an increase in product performance, a decrease in the cost of production and/or improved operation efficiency of the new chemical substance in comparison to existing chemical substances used in similar application; or (6) the extent to which the new chemical substance may be a substitute for an existing substance that poses a greater overall risk to human health or the environment.

☐ Mark (X) this box if you attach a continuation sheet.

Part III -- LIST OF ATTACHMENTS

Attach continuation sheets for sections of the form and test data and other data (including physical/chemical properties and structure/activity information), and optional information after this page. Clearly identify the attachment and the section of the form to which it relates, if appropriate. Number consecutively the pages of the attachments. In the column below, enter the inclusive page numbers of each attachment.
Mark (X) the "Confidential" box next to any attachment name you claim as confidential. Read the Instructions Manual for guidance on how to claim any information in an attachment as confidential. You must include with the sanitized copy of the notice form a sanitized version of any attachment in which you claim information as confidential.

Attachment name	Attachment page number(s)	Confi-dential
1. Material Safety Data Sheets for the PMN Substance	14-43	
2. Continuation Sheet for Part I, Section B, 1.e., Chemical Identity Information	44-46	
3. Toxicity Review and Hazard Assessment of the PMN Substance	47-53	
		X
		X
		X
		X
		X
		X
		X
		X
		X
		X
		X

☐ Mark (X) this box if you attach a continuation sheet. Enter the attachment name and number.

PHYSICAL AND CHEMICAL PROPERTIES WORKSHEET

To assist EPA's review of physical and chemical properties data, please complete the following worksheet for data you provide and include it in the notice. Identify the property measured, the page of the notice on which the property appears, the value of the property, the units in which the property is measured (as necessary), and whether or not the property is claimed as confidential. The physical state of the neat substance should be provided. These measured properties should be for the neat (100% pure) chemical substance. Properties that are measured for mixtures or formulations should be so noted (% PMN substance in __). You are not required to submit this worksheet; however, EPA strongly recommends that you do so, as it will simplify review and ensure that confidential information is properly protected. You should submit this worksheet as a supplement to your submission of test data. This worksheet is not a substitute for submission of test data.

Property (a)	Mark (X) if provided	Page number (b)	Value (c)	Measured or Estimate (M or E)	Confi-dential Mark (X) (d)
Physical state of neat substance	X		X (s) __ (l) __ (g)	M	
Vapor pressure @ Temperature _____°C			Torr		
Density/relative density			g/cm3		
Solubility @ Temperature _____°C Solvent _____			Insoluble in water. Not soluble in solvents. The PMN substance does form stable suspensions in dimethylformamide (after high power sonication) but in very limited quantity (about 1-10 mg/L).	E	
Solubility in water @ Temperature _____°C			g/L		
Melting temperature			°C		
Boiling / sublimation temperature@_____torr pressure			°C		
Spectra					
Specific Gravity			2.0 g/cm^3	E	
Particle size distribution	X		[redacted]	M	X
Young's Modulus	X		[redacted]	E	
Surface area	X		[redacted]	M	X
Mean Number of Walls	X		[redacted]	M	X
Outer Mean Diameter	X		[redacted]	M	X
Outer Diameter Distribution	X		[redacted]	M	X
Inner Mean Diameter	X		[redacted]	M	X
Inner Diameter Distribution	X		[redacted]	M	X
Bulk Density	X		[redacted]	M	X
Agglomeration/Aggregation State	X		[redacted]	M	X
Tensile Strength	X		[redacted]	E	
Molecular Weight	X		[redacted]	M	X

[redacted]

Material Safety Data Sheet

[redacted]

1. PRODUCT AND COMPANY IDENTIFICATION

Company

[redacted]

Customer Service Telephone Number: [redacted]

Emergency Information

Transportation: CHEMTREC: (800) 424-9300
(24 hrs., 7 days a week)

Medical: Rocky Mountain Poison Center: (303) 623-5716
(24 hrs., 7 days a week)

Product Information

Product name: [redacted]
Synonyms:
Molecular formula:
Chemical family:
Product use:

2. HAZARDS IDENTIFICATION

Emergency Overview

Color: black
Physical state: solid
Form: powder
Odor: none

WARNING!
MAY FORM COMBUSTIBLE DUST AIR MIXTURES.
MAY CAUSE EYE, SKIN AND RESPIRATORY TRACT IRRITATION.

Potential Health Effects

Primary routes of exposure:
Inhalation and skin contact.

Signs and symptoms of acute exposure:
Dust: May cause eye irritation. May cause irritation of respiratory tract. Prolonged or repeated contact may dry skin and cause irritation.

[redacted] Material Safety Data Sheet [redacted]

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS-No.	Wt/Wt	OSHA Hazardous
[redacted]	[redacted]		

The substance(s) marked with a "Y" in the Hazard column above, are those identified as hazardous chemicals under the criteria of the OSHA Hazard Communication Standard (29 CFR 1910.1200).

This material is classified as hazardous under Federal OSHA regulation.

4. FIRST AID MEASURES

Inhalation:
If inhaled, remove victim to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Skin:
In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation persists. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Eyes:
Immediately flush eye(s) with plenty of water. Get medical attention if irritation persists.

Ingestion:
If swallowed, DO NOT induce vomiting. Get medical attention. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Flash point: Not determined

Auto-ignition temperature: > 752 °F (> 400 °C) (Method: Standard NF EN 50281-2-1)

Lower flammable limit (LFL): Not determined

Upper flammable limit (UFL): Not determined

Extinguishing media (suitable):
Water spray, Carbon dioxide (CO2), Dry powder

Protective equipment:
Fire fighters and others who may be exposed to products of combustion should wear full fire fighting turn out gear (full Bunker Gear) and self-contained breathing apparatus (pressure demand / NIOSH approved or equivalent). Fire fighting equipment should be thoroughly decontaminated after use.

Further firefighting advice:
Do not use a solid stream of water.
A solid stream of water can cause a dust explosion.

Fire and explosion hazards:
Dust clouds generated during handling and/or storage can form explosive mixtures with air. Dust explosion characteristics vary with the particle size, particle shape, moisture content, contaminants, and other variables.
Note: Check that all equipment is properly grounded and installed to satisfy electrical classification requirements. As with any dry material, pouring this material or allowing it to free-fall or to be conveyed through chutes or pipes can accumulate and generate electrostatic sparks, potentially causing ignition of the material itself, or of any flammable materials which may come into contact with the material or its container.

6. ACCIDENTAL RELEASE MEASURES

In case of spill or leak:
Sweep up and shovel into suitable containers for disposal. Use only non-sparking tools. Wet down dust with water spray jet. Spills should be contained and placed in suitable containers for disposal. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits.

7. HANDLING AND STORAGE

Handling

General information on handling:
Keep away from heat, sparks and flames.
Avoid contact with the skin, eyes and clothing.
Avoid breathing dust.
Keep container closed.
Avoid creating dust in handling, transfer or clean up.
Prevent dust accumulation.
Check that all equipment is properly grounded and installed to satisfy electrical classification requirements.
Use only with adequate ventilation.
Wash thoroughly after handling.
Container hazardous when empty.
Emptied container retains product residue.
Follow label warnings even after container is emptied.
RESIDUAL DUSTS MAY EXPLODE ON IGNITION.
DO NOT CUT, DRILL, GRIND, OR WELD ON OR NEAR THIS CONTAINER.
Improper disposal or reuse of this container may be dangerous and/or illegal.

Storage

General information on storage conditions:
Store in cool, dry, well ventilated area away from sources of ignition such as flame, sparks and static electricity. Ensure that all storage and handling equipment is properly grounded and installed to satisfy electrical classification requirements. Static electricity may accumulate when transferring material. All storage containers, including drums, cylinders and IBCs, must be bonded and grounded during filling and emptying operations.

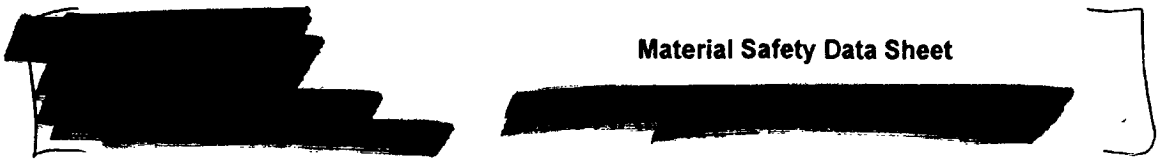
Storage incompatibility – General:
Store separate from oxidizers.

Storage incompatibility – Segregation (specific):
Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Airborne Exposure Guidelines:

[redacted]



Only those components with exposure limits are printed in this section. Limits with skin contact designation above have skin contact effect. Air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required. Limits with a sensitizer designation above mean that exposure to this material may cause allergic reactions.

Engineering controls:
Investigate engineering techniques to reduce exposures below airborne exposure limits. Provide ventilation if necessary to control exposure levels below airborne exposure limits (see above). If practical, use local mechanical exhaust ventilation at sources of air contamination such as open process equipment. Consult ACGIH ventilation manual or NFPA Standard 91 for design of exhaust systems.

Respiratory protection:
Avoid breathing dust. Where airborne exposure is likely or airborne exposure limits are exceeded (if applicable, see above), use NIOSH approved respiratory protection equipment appropriate to the material and/or its components (full facepiece recommended). Consult respirator manufacturer to determine appropriate type equipment for a given application. Observe respirator use limitations specified by NIOSH or the manufacturer. For emergency and other conditions where there may be a potential for significant exposure or where exposure limit may be significantly exceeded, use an approved full face positive-pressure, self-contained breathing apparatus or positive-pressure airline with auxiliary self-contained air supply. Respiratory protection programs must comply with 29 CFR § 1910.134.

Skin protection:
Wear appropriate chemical resistant protective clothing and chemical resistant gloves to prevent skin contact. Consult glove manufacturer to determine appropriate type glove material for given application. Rinse immediately if skin is contaminated. Wash contaminated clothing and clean protective equipment before reuse. Wash thoroughly after handling.

Eye protection:
Where eye contact may be likely, wear chemical goggles and have eye flushing equipment available.

9. PHYSICAL AND CHEMICAL PROPERTIES

Color:	black
Physical state:	solid
Form:	powder
Odor:	none
pH:	no data available
Density:	no data available
Specific Gravity (Relative density):	no data available
Bulk density:	100 - 400 kg/m3
Vapor pressure:	no data available
Vapor density:	no data available

Boiling point/boiling range:	no data available
Freezing point:	no data available
Melting point/range:	no data available
Solubility in water:	insoluble

10. STABILITY AND REACTIVITY

Stability:
This material is chemically stable under normal and anticipated storage, handling and processing conditions.

Materials to avoid:
Strong oxidizing agents

Conditions / hazards to avoid:
To avoid thermal decomposition, do not overheat.

Hazardous decomposition products:
Thermal decomposition giving toxic products :
Carbon oxides

11. TOXICOLOGICAL INFORMATION

[redacted]

Acute toxicity

Oral:
Practically nontoxic. (rat) LD50 > 5,000 mg/kg.

Skin Irritation:
Non-irritating. (rabbit)

Eye Irritation:
Non-irritating. (rabbit)

[redacted]

Acute toxicity

Oral:
Slightly toxic. (rat) LD50 = 1,600 mg/kg.

Dermal:
No more than slightly toxic. (rabbit) LD50 > 1,000 mg/kg.

Carcinogenicity

Chronic inhalation, intratracheal injection administration to rat, mouse, hamster, guinea pig / No increase in tumor incidence was reported.

[redacted]

Carcinogenicity
Repeated inhalation, intratracheal injection administration to rat / affected organ(s): lung / signs: fibrosis

Human experience
Inhalation:
Respiratory tract: Epidemiology studies of workers indicate pulmonary function is not affected; no significant increases in cancer.

[redacted]

Acute toxicity

Oral:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

Dermal:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

Skin Irritation:
Slightly irritating. (rabbit)

Eye Irritation:
Moderately irritating. (rabbit)

Other routes:

[redacted]

Skin Sensitization:
Not a skin sensitizer. (mouse)

Genotoxicity

Assessment in Vitro:
No genetic changes were observed in laboratory tests using: bacteria, human cells

12. ECOLOGICAL INFORMATION

Chemical Fate and Pathway
No data are available.

Ecotoxicology

[redacted]

Aquatic toxicity data:

Practically nontoxic. Leuciscus idus (Golden orfe) 48 h LC0 = 1,000 mg/l

Microorganisms:
Practically nontoxic. Bacteria EC0 = 5,000 mg/l

13. DISPOSAL CONSIDERATIONS

Waste disposal:
Where possible recycling is preferred to disposal or incineration. If recycling is not an option, incinerate or dispose of in accordance with federal, state, and local regulations. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits. Note: Chemical additions to, processing of, or otherwise altering this material may make this waste management information incomplete, inaccurate, or otherwise inappropriate. Furthermore, state and local waste disposal requirements may be more restrictive or otherwise different from federal laws and regulations.

14. TRANSPORT INFORMATION

US Department of Transportation (DOT): not regulated

International Maritime Dangerous Goods Code (IMDG): not regulated

15. REGULATORY INFORMATION

Chemical Inventory Status

EU. EINECS	EINECS	Conforms to
US. Toxic Substances Control Act	TSCA	The components of this product are all on the TSCA Inventory.
Australia. Industrial Chemical (Notification and Assessment) Act	AICS	Conforms to
Canada. Canadian Environmental Protection Act (CEPA). Domestic Substances List (DSL). (Can. Gaz. Part II, Vol. 133)	DSL	All components of this product are on the Canadian DSL list.
Japan. Kashin-Hou Law List	ENCS (JP)	Conforms to
Korea. Toxic Chemical Control Law (TCCL) List	KECI (KR)	Conforms to
Philippines. The Toxic Substances and Hazardous and Nuclear Waste Control Act	PICCS (PH)	Conforms to
China. Inventory of Existing Chemical Substances	INV (CN)	Conforms to
New Zealand. Inventory of Chemicals (NZIoC), as published by ERMA New Zealand	NZIOC	Conforms to

[redacted] **Material Safety Data Sheet** [redacted]

United States – Federal Regulations

SARA Title III – Section 302 Extremely Hazardous Chemicals:
SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA Title III - Section 311/312 Hazard Categories:
Acute Health Hazard

SARA Title III – Section 313 Toxic Chemicals:

Chemical Name	CAS-No.	De minimis concentration	Reportable threshold:
[redacted]	[redacted]		[redacted]

Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) - Reportable Quantity (RQ):

The components in this product are either not CERCLA regulated, regulated but present in negligible concentrations or regulated with no assigned reportable quantity.

OSHA Regulated Carcinogens (NTP, IARC, OSHA Listed):

NTP:
No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

IARC:
No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA:
No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

United States – State Regulations

Massachusetts Right to Know

Chemical Name	CAS-No
[redacted]	[redacted]

[redacted] **Material Safety Data Sheet** [redacted]

New Jersey Right to Know

Chemical Name	CAS-No
[redacted]	[redacted]

Pennsylvania Right to Know

Chemical Name	CAS-No
[redacted]	[redacted]

Pennsylvania Right to Know – Environmentally Hazardous Substance(s)

Chemical Name	CAS-No
[redacted]	

California Prop. 65
This product does not contain any chemicals known to the State of California to cause cancer, birth defects, or any other reproductive effects.

16. OTHER INFORMATION

Latest Revision(s):

Reference number: 000000047038
Date of Revision: 07/25/2008
Date Printed: 09/18/2008

[redacted]

[redacted]

Material Safety Data Sheet

[redacted]

1. PRODUCT AND COMPANY IDENTIFICATION

Company

[redacted]

Customer Service Telephone Number: [redacted]

Emergency Information

Transportation: CHEMTREC: (800) 424-9300
(24 hrs., 7 days a week)

Medical: Rocky Mountain Poison Center: (303) 623-5716
(24 hrs., 7 days a week)

Product Information

Product name: [redacted]
Synonyms:
Molecular formula:
Chemical family:
Product use: Additive in coatings, composities, and thermoplastic polymers.

2. HAZARDS IDENTIFICATION

Emergency Overview

Color: black
Physical state: solid
Form: powder
Odor: none

WARNING!
MAY FORM COMBUSTIBLE DUST AIR MIXTURES.
MAY CAUSE EYE, SKIN AND RESPIRATORY TRACT IRRITATION.

Potential Health Effects

Primary routes of exposure:
Inhalation and skin contact.

Signs and symptoms of acute exposure:
Dust: May cause eye irritation. May cause irritation of respiratory tract. Prolonged or repeated contact may dry skin and cause irritation.

[redacted] **Material Safety Data Sheet** [redacted]

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS-No.	Wt/Wt	OSHA Hazardous
[redacted]	[redacted]	[redacted]	[redacted]

The substance(s) marked with a "Y" in the Hazard column above, are those identified as hazardous chemicals under the criteria of the OSHA Hazard Communication Standard (29 CFR 1910.1200).

This material is classified as hazardous under Federal OSHA regulation.

4. FIRST AID MEASURES

Inhalation:
If inhaled, remove victim to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

Skin:
In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation persists. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Eyes:
Immediately flush eye(s) with plenty of water. Get medical attention if irritation persists.

Ingestion:
If swallowed, DO NOT induce vomiting. Get medical attention. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Flash point: no data available

Auto-ignition temperature: no data available

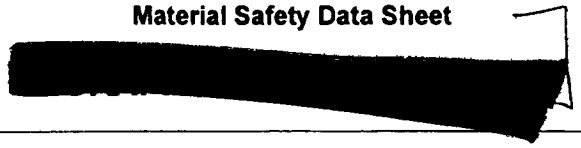
Lower flammable limit (LFL): no data available

Upper flammable limit (UFL): no data available

Extinguishing media (suitable):
Water spray, Carbon dioxide (CO2), Dry powder

Protective equipment:
Fire fighters and others who may be exposed to products of combustion should wear full fire fighting turn out gear (full Bunker Gear) and self-contained breathing apparatus (pressure demand / NIOSH approved or equivalent). Fire fighting equipment should be thoroughly decontaminated after use.

Further firefighting advice:



A solid stream of water can cause a dust explosion.
Do not use a solid stream of water.

Fire and explosion hazards:
Dust clouds generated during handling and/or storage can form explosive mixtures with air. Dust explosion characteristics vary with the particle size, particle shape, moisture content, contaminants, and other variables.
Note: Check that all equipment is properly grounded and installed to satisfy electrical classification requirements. As with any dry material, pouring this material or allowing it to free-fall or to be conveyed through chutes or pipes can accumulate and generate electrostatic sparks, potentially causing ignition of the material itself, or of any flammable materials which may come into contact with the material or its container.

6. ACCIDENTAL RELEASE MEASURES

In case of spill or leak:
Sweep up and shovel into suitable containers for disposal. Use only non-sparking tools. Wet down dust with water spray jet. Spills should be contained and placed in suitable containers for disposal. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits.

7. HANDLING AND STORAGE

Handling

General information on handling:
Keep away from heat, sparks and flames.
Avoid contact with the skin, eyes and clothing.
Avoid breathing dust.
Keep container closed.
Avoid creating dust in handling, transfer or clean up.
Prevent dust accumulation.
Check that all equipment is properly grounded and installed to satisfy electrical classification requirements.
Use only with adequate ventilation.
Wash thoroughly after handling.
Container hazardous when empty.
Emptied container retains product residue.
Follow label warnings even after container is emptied.
RESIDUAL DUSTS MAY EXPLODE ON IGNITION.
DO NOT CUT, DRILL, GRIND, OR WELD ON OR NEAR THIS CONTAINER.
Improper disposal or reuse of this container may be dangerous and/or illegal.

Storage

General information on storage conditions:
Store in well ventilated area away from heat and sources of ignition such as flame, sparks and static electricity. Ensure that all storage and handling equipment is properly grounded and installed to satisfy electrical classification requirements. Static electricity may accumulate when transferring material. All storage containers, including drums, cylinders and IBCs, must be bonded and grounded during filling and emptying operations.

Storage incompatibility – General:
Store separate from oxidizers.

Storage incompatibility – Segregation (specific):
Strong oxidizing agents

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

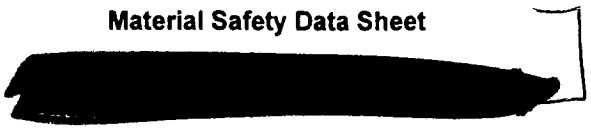
Airborne Exposure Guidelines:

[redacted]

Only those components with exposure limits are printed in this section. Limits with skin contact designation above have skin contact effect. Air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required. Limits with a sensitizer designation above mean that exposure to this material may cause allergic reactions.

Engineering controls:
Investigate engineering techniques to reduce exposures below airborne exposure limits. Provide ventilation if necessary to control exposure levels below airborne exposure limits (see above). If practical, use local mechanical exhaust ventilation at sources of air contamination such as open process equipment. Consult ACGIH ventilation manual or NFPA Standard 91 for design of exhaust systems.

Respiratory protection:
Avoid breathing dust. Where airborne exposure is likely or airborne exposure limits are exceeded (if applicable, see above), use NIOSH approved respiratory protection equipment appropriate to the material and/or its components (full facepiece recommended). Consult respirator manufacturer to determine appropriate type



equipment for a given application. Observe respirator use limitations specified by NIOSH or the manufacturer. For emergency and other conditions where there may be a potential for significant exposure or where exposure limit may be significantly exceeded, use an approved full face positive-pressure, self-contained breathing apparatus or positive-pressure airline with auxiliary self-contained air supply. Respiratory protection programs must comply with 29 CFR § 1910.134.

Skin protection:
Wear appropriate chemical resistant protective clothing and chemical resistant gloves to prevent skin contact. Consult glove manufacturer to determine appropriate type glove material for given application. Rinse immediately if skin is contaminated. Wash contaminated clothing and clean protective equipment before reuse. Wash thoroughly after handling.

Eye protection:
Where eye contact may be likely, wear chemical goggles and have eye flushing equipment available.

9. PHYSICAL AND CHEMICAL PROPERTIES

Color:	black
Physical state:	solid
Form:	powder
Odor:	none
pH:	no data available
Density:	no data available
Specific Gravity (Relative density):	no data available
Bulk density:	100 - 400 kg/m3
Vapor pressure:	no data available
Vapor density:	no data available
Boiling point/boiling range:	no data available
Freezing point:	no data available
Melting point/range:	no data available
Solubility in water:	insoluble

10. STABILITY AND REACTIVITY

Stability:
This material is chemically stable under normal and anticipated storage, handling and processing conditions.

Materials to avoid:
Strong oxidizing agents

Conditions / hazards to avoid:
To avoid thermal decomposition, do not overheat.

Hazardous decomposition products:
Thermal decomposition giving toxic products :
Carbon oxides

11. TOXICOLOGICAL INFORMATION

Data on this material and/or its components are summarized below

[redacted]

Acute toxicity

Oral:
Slightly toxic. (rat) LD50 = 1,600 mg/kg.

Dermal:
No more than slightly toxic. (rabbit) LD50 > 1,000 mg/kg.

Carcinogenicity
Chronic inhalation, intratracheal injection administration to rat, mouse, hamster, guinea pig / No increase in tumor incidence was reported.

[redacted]

Carcinogenicity
Repeated inhalation, intratracheal injection administration to rat / affected organ(s): lung / signs: fibrosis

Human experience
Inhalation:
Respiratory tract: Epidemiology studies of workers indicate pulmonary function is not affected; no significant increases in cancer.

[redacted]

Acute toxicity

Oral:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

Dermal:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

[redacted] Material Safety Data Sh[redacted]

Skin Irritation:
Slightly irritating. (rabbit)

Eye Irritation:
Moderately irritating. (rabbit)

Other routes:

[redacted]

Skin Sensitization:
Not a skin sensitizer. (mouse)

Genotoxicity

Assessment in Vitro:
No genetic changes were observed in laboratory tests using: bacteria, human cells

12. ECOLOGICAL INFORMATION

Chemical Fate and Pathway
No data are available.

Ecotoxicology
Data on this material and/or its components are summarized below.

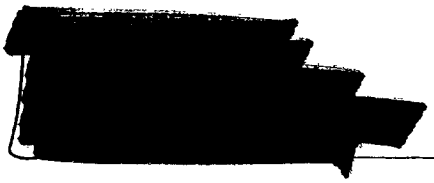
[redacted]

Aquatic toxicity data:
Practically nontoxic. Leuciscus idus (Golden orfe) 48 h LC0 = 1,000 mg/l

Microorganisms:
Practically nontoxic. Bacteria EC0 = 5,000 mg/l

13. DISPOSAL CONSIDERATIONS

Waste disposal:
Where possible recycling is preferred to disposal or incineration. If recycling is not an option, incinerate or dispose of in accordance with federal, state, and local regulations. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits. Note: Chemical additions to, processing of, or otherwise altering this material may make this waste management information incomplete, inaccurate, or otherwise inappropriate. Furthermore, state and local waste disposal requirements may be more restrictive or otherwise different from federal laws and regulations.



14. TRANSPORT INFORMATION

US Department of Transportation (DOT): not regulated

International Maritime Dangerous Goods Code (IMDG): not regulated

15. REGULATORY INFORMATION

Chemical Inventory Status

EU. EINECS	EINECS	Conforms to
US. Toxic Substances Control Act	TSCA	The components of this product are all on the TSCA Inventory.
Australia. Industrial Chemical (Notification and Assessment) Act	AICS	Conforms to
Canada. Canadian Environmental Protection Act (CEPA). Domestic Substances List (DSL). (Can. Gaz. Part II, Vol. 133)	DSL	All components of this product are on the Canadian DSL list.
Japan. Kashin-Hou Law List	ENCS (JP)	Conforms to
Korea. Toxic Chemical Control Law (TCCL) List	KECI (KR)	Conforms to
Philippines. The Toxic Substances and Hazardous and Nuclear Waste Control Act	PICCS (PH)	Conforms to
China. Inventory of Existing Chemical Substances	IECSC (CN)	Conforms to
New Zealand. Inventory of Chemicals (NZIoC), as published by ERMA New Zealand	NZIOC	Conforms to

United States – Federal Regulations

SARA Title III – Section 302 Extremely Hazardous Chemicals:
SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA Title III - Section 311/312 Hazard Categories:
Acute Health Hazard

SARA Title III – Section 313 Toxic Chemicals:
SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) - Reportable Quantity (RQ):

The components in this product are either not CERCLA regulated, regulated but present in negligible concentrations, or regulated with no assigned reportable quantity.

OSHA Regulated Carcinogens (NTP, IARC, OSHA Listed):

NTP:
No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

IARC:
No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA:
No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

United States – State Regulations

Massachusetts Right to Know

Chemical Name	CAS-No.
[redacted]	[redacted]

New Jersey Right to Know

Chemical Name	CAS-No.
[redacted]	[redacted]

Pennsylvania Right to Know

Chemical Name	CAS-No.
[redacted]	[redacted]

California Prop. 65
This product does not contain any chemicals known to the State of California to cause cancer, birth defects, or any other reproductive effects.

16. OTHER INFORMATION

Latest Revision(s):

Reference number:	000000054675
Date of Revision:	07/25/2008
Date Printed:	07/25/2008

[redacted]

[redacted]

[redacted]

[redacted] **Material Safety Data Sheet** [redacted]

1. PRODUCT AND COMPANY IDENTIFICATION

Company

[redacted]

Emergency Information

Transportation: CHEMTREC: (800) 424-9300
(24 hrs., 7 days a week)

Medical: Rocky Mountain Poison Center: (303) 623-5716
(24 hrs., 7 days a week)

Product Information

Product name: [redacted]
Synonyms:
Molecular formula:
Chemical family:
Product use: [redacted]sives

2. HAZARDS IDENTIFICATION

Emergency Overview

Color: black
Physical state: liquid
Odor: slight

WARNING!
MAY CAUSE SKIN IRRITATION.
MAY CAUSE ALLERGIC SKIN REACTION.

Potential Health Effects

Primary routes of exposure:
Inhalation and skin contact.

Signs and symptoms of acute exposure:
May cause skin irritation. Allergic skin reaction: redness, rash.

Skin:
Practically nontoxic. Moderately irritating. (based on components)

Eyes:
Slightly irritating. (based on components)

Ingestion:
Practically nontoxic. (based on components)

3. COMPOSITION/INFORMATION ON INGREDIENTS

Chemical Name	CAS-No.	Wt/Wt	OSHA Hazardous
[redacted]			

The substance(s) marked with a "Y" in the Hazard column above, are those identified as hazardous chemicals under the criteria of the OSHA Hazard Communication Standard (29 CFR 1910.1200).

This material is classified as hazardous under Federal OSHA regulation

4. FIRST AID MEASURES

Inhalation:
If inhaled, remove to fresh air.

Skin:
In case of contact, immediately flush skin with soap and plenty of water. Remove contaminated clothing and shoes. Get medical attention if symptoms occur. Wash clothing before reuse. Thoroughly clean shoes before reuse.

Eyes:
Immediately flush eye(s) with plenty of water.

Ingestion:
If swallowed, DO NOT induce vomiting. Get medical attention. Never give anything by mouth to an unconscious person.

5. FIRE-FIGHTING MEASURES

Flash point: > 392 °F (> 200 °C) (closed cup)

Auto-ignition temperature: Not determined

Lower flammable limit (LFL): Not determined

Upper flammable limit (UFL): Not determined

Extinguishing media (suitable):
Carbon dioxide (CO2), Dry powder, Water spray

Protective equipment:

Fire fighters and others who may be exposed to products of combustion should wear full fire fighting turn out gear (full Bunker Gear) and self-contained breathing apparatus (pressure demand / NIOSH approved or equivalent).

Further firefighting advice:
Fire fighting equipment should be thoroughly decontaminated after use.

Fire and explosion hazards:
When burned, the following hazardous products of combustion can occur:
Carbon oxides

6. ACCIDENTAL RELEASE MEASURES

In case of spill or leak:
Spills should be contained and placed in suitable containers for disposal. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits.

7. HANDLING AND STORAGE

Handling

General information on handling:
Wash thoroughly after handling.
Avoid contact with the skin, eyes and clothing.
Emptied container retains vapor and product residue.
Observe all labeled safeguards until container is cleaned, reconditioned or destroyed.

Storage

General information on storage conditions:
Keep containers tightly closed in a dry, cool and well-ventilated place.

Storage stability – Temperature:–
36 - 104 °F (2 - 40 °C)

Storage incompatibility – General:
Store separate from strong acids, strong bases, and strong oxidizing agents.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Airborne Exposure Guidelines:

[redacted] Material Safety Data Sheet [redacted]

[redacted]

Only those components with exposure limits are printed in this section. Limits with skin contact designation above have skin contact effect. Air sampling alone is insufficient to accurately quantitate exposure. Measures to prevent significant cutaneous absorption may be required. Limits with a sensitizer designation above mean that exposure to this material may cause allergic reactions.

Engineering controls:
Investigate engineering techniques to reduce exposures. Provide ventilation if necessary to control exposure levels below airborne exposure limits (see above). If practical, use local mechanical exhaust ventilation at sources of air contamination such as open process equipment.

Respiratory protection:
Avoid breathing vapor or mist. Where airborne exposure is likely or airborne exposure limits are exceeded (if applicable, see above), use NIOSH approved respiratory protection equipment appropriate to the material and/or its components (full facepiece recommended). Consult respirator manufacturer to determine appropriate type equipment for a given application. Observe respirator use limitations specified by NIOSH or the manufacturer. For emergency and other conditions where there may be a potential for significant exposure or where exposure limit may be significantly exceeded, use an approved full face positive-pressure, self-contained breathing apparatus or positive-pressure airline with auxiliary self-contained air supply. Respiratory protection programs must comply with 29 CFR § 1910.134.

Skin protection:
Wear appropriate chemical resistant protective clothing and chemical resistant gloves to prevent skin contact. When handling this material, gloves of the following type(s) should be worn:

Neoprene

Nitrile rubber

Impervious butyl rubber gloves

Wear face shield and chemical resistant clothing such as a rubber apron when splashing may occur. Rinse immediately if skin is contaminated. Wash contaminated clothing and clean protective equipment before reuse. Wash thoroughly after handling.

Eye protection:
Use good industrial practice to avoid eye contact.

9. PHYSICAL AND CHEMICAL PROPERTIES

Color:	black
Physical state:	liquid

Odor:	slight
pH:	not determined
Density:	1,150 - 1,200 kg/m3 77 °F (25 °C)
Vapor pressure:	not determined
Vapor density:	not determined
Boiling point/boiling range:	> 392 °F (> 200 °C)
Melting point/range:	> 392 °F (> 200 °C)
Solubility in water:	< 1 mg/l

10. STABILITY AND REACTIVITY

Stability:
This material is chemically stable under normal and anticipated storage, handling and processing conditions.

Materials to avoid:
Strong oxidizing agents
Strong acids
strong bases

Conditions / hazards to avoid:
Keep away from heat and sources of ignition. To avoid thermal decomposition, do not overheat.

Hazardous decomposition products:
Thermal decomposition giving toxic products :
Carbon oxides

11. TOXICOLOGICAL INFORMATION

[redacted]

Acute toxicity

Oral:
Practically nontoxic. (rat) LD50 > 5,000 mg/kg.

Dermal:
Practically nontoxic. (rabbit) LD50 > 6,000 mg/kg.

Skin Irritation:
Moderately irritating. (rabbit)

Eye Irritation:
Slightly irritating. (rabbit)

Skin Sensitization:
Repeated skin exposure. (laboratory animal) Skin allergy was observed.

Genotoxicity

Assessment in Vitro:
Both positive and negative reponses for genetic changes were observed in laboratory tests using: bacteria

Genotoxicity

Assessment in Vivo:
No genetic changes were observed in laboratory tests using: animals, rodent

Developmental toxicity
Exposure during pregnancy. (rat and rabbit) / No birth defects were observed.

Human experience
Skin contact:
Skin: Skin allergy was observed.

[redacted]

Carcinogenicity
Repeated inhalation, intratracheal injection administration to rat / affected organ(s): lung / signs: fibrosis

Human experience
Inhalation:
Respiratory tract: Epidemiology studies of workers indicate pulmonary function is not affected; no significant increases in cancer.

[redacted]

Acute toxicity

Oral:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

Dermal:
No more than slightly toxic. (rat) LD50 > 2,000 mg/kg.

Skin Irritation:
Slightly irritating. (rabbit)

Eye Irritation:
Moderately irritating. (rabbit)

Other routes:

[redacted]

[redacted]

Skin Sensitization:
Not a skin sensitizer. (mouse)

Genotoxicity

Assessment in Vitro:
No genetic changes were observed in laboratory tests using: bacteria, human cells

12. ECOLOGICAL INFORMATION

Chemical Fate and Pathway
Data on this material and/or its components are summarized below.

[redacted]

Biodegradation:
Not readily biodegradable (28 d) biodegradation 2 - 3 %

Octanol Water Partition Coefficient:
log Pow ca. 3.8

Ecotoxicology
Data on this material and/or its components are summarized below.

[redacted]

Aquatic toxicity data:
Practically nontoxic. Oncorhynchus mykiss (rainbow trout) LC50 > 1,000 mg/l

13. DISPOSAL CONSIDERATIONS

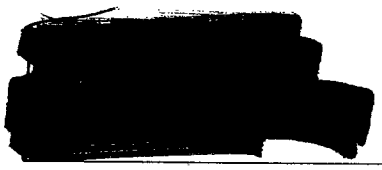
Waste disposal:
Where possible recycling is preferred to disposal or incineration. If recycling is not an option, incinerate or dispose of in accordance with federal, state, and local regulations. Consult a regulatory specialist to determine appropriate state or local reporting requirements, for assistance in waste characterization and/or hazardous waste disposal and other requirements listed in pertinent environmental permits. Note: Chemical additions to, processing of, or otherwise altering this material may make this waste management information incomplete, inaccurate, or otherwise inappropriate. Furthermore, state and local waste disposal requirements may be more restrictive or otherwise different from federal laws and regulations.

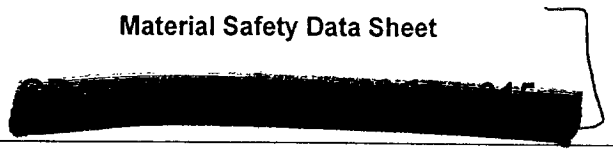
14. TRANSPORT INFORMATION

US Department of Transportation (DOT): not regulated

International Maritime Dangerous Goods Code (IMDG)

UN Number	:	3082
Proper shipping name	:	ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S.





Technical name	:	(EPOXY RESIN)
Class	:	9
Packaging group	:	III
Marine pollutant	:	no
Flash point	:	> 392 °F (> 200 °C) closed cup

15. REGULATORY INFORMATION

Chemical Inventory Status

EU. EINECS	EINECS	Conforms to
US. Toxic Substances Control Act	TSCA	The components of this product are all on the TSCA Inventory.
Australia. Industrial Chemical (Notification and Assessment) Act	AICS	Conforms to
Canada. Canadian Environmental Protection Act (CEPA). Domestic Substances List (DSL). (Can. Gaz. Part II, Vol. 133)	DSL	All components of this product are on the Canadian DSL list.
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Philippines. The Toxic Substances and Hazardous and Nuclear Waste Control Act	PICCS (PH)	Conforms to
China. Inventory of Existing Chemical Substances	IECSC (CN)	Conforms to

United States – Federal Regulations

SARA Title III – Section 302 Extremely Hazardous Chemicals:
SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA Title III - Section 311/312 Hazard Categories:
Acute Health Hazard

SARA Title III – Section 313 Toxic Chemicals:
SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) - Reportable Quantity (RQ):

The components in this product are either not CERCLA regulated, regulated but present in negligible concentrations, or regulated with no assigned reportable quantity.

[redacted] Material Safety Data Sheet [redacted]

OSHA Regulated Carcinogens (NTP, IARC, OSHA Listed):

NTP:
No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

IARC:
No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA:
No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

United States – State Regulations

Massachusetts Right to Know

Chemical Name [redacted] CAS-No. [redacted]

New Jersey Right to Know

No components are subject to the New Jersey Right to Know Act.

Pennsylvania Right to Know

Chemical Name [redacted] CAS-N[redacted]

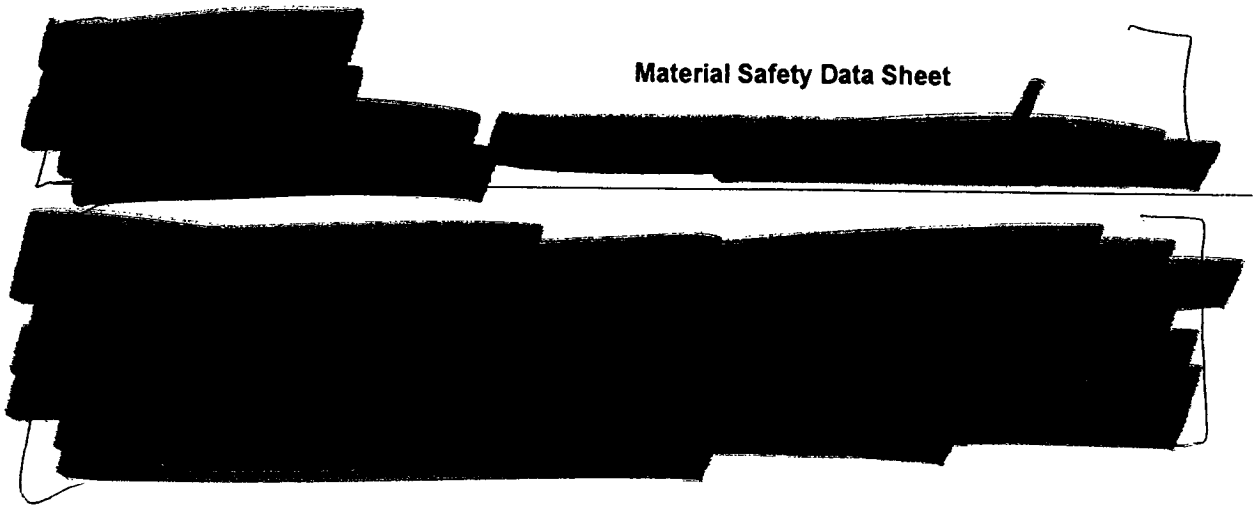
California Prop. 65
This product does not contain any chemicals known to the State of California to cause cancer, birth defects, or any other reproductive effects.

16. OTHER INFORMATION

Latest Revision(s):

Revised Section(s): [redacted]
Reference number: [redacted]
Date of Revision: 07/25/2008
Date Printed: 09/18/2008

[redacted]


Material Safety Data Sheet

Pages 44– 103
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CONFIDENTIAL

Safety & Health
Research Laboratories

SPONSOR

[redacted]

[redacted]

STUDY TITLE

ACUTE ORAL TOXICITY IN RATS
"ACUTE TOXIC CLASS METHOD"

STUDY DIRECTOR

Catherine Pelcot

DATE OF ISSUE

25 April 2008

TEST FACILITY

CIT
BP 563 - 27005 Evreux - France

[redacted]

IFM Recherche
S.N.C au Capital de 846 092 €
788 060 465 R.C.S. Evreux
VAT FR19 788 060 465
Agrément Crédit Impôt Recherche

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E-mail : CIT@citox.com
Web site : www.citox.com

CONTENTS

[redacted] 3

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with CIT's standard operating procedures and the following principles of Good Laboratory Practice:

- OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents.
- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20.2.2004).
- Décret N° 2006-1523 du 04 décembre 2006 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 06 décembre 2006), Ministère de l'Economie, des Finances et de l'Industrie.

However, no chemical analysis of the dosage forms was performed as part of this study.
This exception is not considered to impact the overall GLP status of the study.

The study was also conducted in compliance with the following Animal Protection regulations:

- Council Directive 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.
- Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation, OECD Environmental Health and Safety Publications, No. 19.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at CIT, BP 563, 27005 Evreux, France.

Toxicology

C. Pelcot
Study Director

Study completion date: 21 April 2008

OTHER CIT SCIENTIST INVOLVED IN THE STUDY

Director of Toxicology
CIT Management

J.J. Legrand Date: 24 April 2008
Doctor of Veterinary Medicine

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT:

The CIT Quality Assurance Unit conducted the inspections detailed below:

Type of inspection	Dates		
	Inspection	Reported to the Study Director	Reported to Management
Study plan	27 July 2007	27 July 2007	02 August 2007
Report	12 February 2008	14 February 2008	10 March 2008

In addition, at about the same time, process-based and facility inspections relevant to this study were carried out by the Quality Assurance Unit.

The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

A. de Cecco
CIT Quality Assurance Unit

Date: 25 Apr 2008

[redacted]

SUMMARY

[redacted]
OECD (No. 423, 17th December 2001) and EC (2004/73/EC, B.1 tris, 29th April 2004) guidelines.
The study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

The test item was prepared in 0.5% methylcellulose and was administered by oral route (gavage), to groups of three fasted female Sprague-Dawley rats.

The study design was as follows:

Dose-level (mg/kg)	Volume (mL/kg)	Female
300	10	3
2000	14.3	3
2000	14.3	3

Clinical signs, mortality and body weight gain were checked for a period of up to 14 days following the single administration of the test item.

All animals were subjected to necropsy.

Results

Dose-level of 300 mg/kg (three females)
No deaths and no clinical signs were noted at this dose-level.

Dose-level of 2000 mg/kg (three females then confirmation on three other females)
No deaths occurred.
Hypoactivity, piloerection and dyspnea were noted in 3/6 animals on day 1.

When compared to CIT historical control animals, a slightly lower body weight gain was noted between day 1 and day 8 in 1/3 females treated at the dose-level of 300 mg/kg, without any relevant consequence at the end of the observation period, and in 1/6 females treated at the dose-level of 2000 mg/kg, between day 8 and day 15. The body weight gain of the other animals treated at the dose-level of 300 or 2000 mg/kg was not affected by treatment with the test item.

At necropsy, no apparent abnormalities were observed in any animal.

[redacted] 8

Conclusion

Under the experimental conditions of this study, the oral LD_0 of the test item [redacted] 2000 mg/kg in rats.

According to the classification criteria laid down in Council Directive 67/548/EEC (and subsequent adaptations), concerning the potential toxicity by oral route, the test item should not be classified.

[redacted]

RESUME

[redacted]

aux lignes directrices de l'OCDE (n° 423, 17 décembre 2001) et de la CEE (2004/73/CEE, B.1 tris, 29 avril 2004).
L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthode

Le produit a été preparé dans de la méthylcellulose à 0,5 % et administré par voie orale (gavage), à des groupes de 3 femelles rats Sprague-Dawley mis à la diète hydrique.

Le schéma de l'étude a été le suivant:

Dose (mg/kg)	Volume (mL/kg)	Femelle
300	10	3
2000	14,3	3
2000	14,3	3

Les signes cliniques, la mortalité et l'évolution pondérale des animaux ont été suivis pendant une période de 14 jours après l'administration unique du produit.

Un examen anatomopathologique a été effectué sur tous les animaux.

Résultats

Dose de 300 mg/kg (3 femelles)
Aucune mortalité et aucun signe clinique ne sont observés à cette dose.

Dose de 2000 mg/kg (3 femelles puis confirmation sur 3 autres femelles)
Aucune mortalité n'est enregistrée.
Hypoactivité, piloérection et dyspnée sont notées chez 3/6 animaux au Jour 1.

En comparaison avec celle des témoins historiques du CIT, l'évolution pondérale est légèrement réduite entre le Jour 1 et le Jour 8 chez 1/3 femelle traitée à la dose de 300 mg/kg, sans aucune conséquence notable à la fin de la période d'observation, et chez 1/6 femelle traitée à la dose de 2000 mg/kg entre le Jour 8 et le Jour 15. L'évolution pondérale des autres animaux traités aux doses de 300 ou 2000 mg/kg n'est pas influencée par le traitement avec le produit.

L'examen macroscopique des principaux organes réalisé chez tous les animaux ne met en évidence aucune anomalie apparente.

[redacted]

Conclusion

Dans les conditions expérimentales de cette étude, la DL 0 orale du produit [redacted]

Selon les critères de classification décrits dans la Directive 67/548/CEE (et ses adaptations), concernant la toxicité aiguë par voie orale, le produit ne devrait pas être classé.

1. INTRODUCTION

The objective of this study was to evaluate the toxicity of the test item following a single oral administration in rats.

In the assessment of the toxic characteristics of a test item, determination of acute oral toxicity is an initial step. It provides information on health hazards likely to arise following a short-term exposure by the oral route in humans and enables the test item to be ranked in different classification systems.

The acute toxic class method is a stepwise procedure.
The test item is administered orally to one group of animals at one of the defined dose-levels, each step using three animals of one sex.
Absence or presence of compound-related mortality of the animals dosed at one step determines the next step, *i.e.*:

- no further testing is needed,
- the next step is performed with the same dose-level,
- the next step is performed at the next higher or the next lower dose-level.

The study was conducted in compliance with:

- EC Directive 2004/73/EC, B.1 tris, 29th April 2004,
- OECD Guideline No. 423, 17th December 2001.

2. MATERIALS AND METHODS

2.1 TEST ITEM

2.1.1 Identification

- name:
- batch number:
- CAS number:
- Description at receipt: black powder
- container: one plastic flask
- date of receipt: 29 June 2007
- storage conditions: at room temperature and protected from humidity
- composition: see analytical certificate
- expiry date: June 2008.

Data relating to the characterization of the test item are documented in a test article description and an analytical certificate (presented in appendix 1) provided by the Sponsor.

2.1.2 Vehicle

The vehicle used was 0.5% methylcellulose: methylcellulose, batch No. 017K0052 (Sigma, Saint-Quentin-Fallavier, France) in purified water (prepared at CIT by reverse osmosis).

2.1.3 Dosage form preparation

The test item was not soluble at the concentration of 100 mg/mL in purified water, 0.5% methylcellulose and corn oil. At the maximal concentration of 70 mg/mL, a suspension was obtained in purified water or in 0.5% methylcellulose. As the suspension was more homogeneous in 05% methylcellulose, this vehicle was retained.

On the day of treatment, the test item was ground to a fine powder using a mortar and pestle, then was prepared at the chosen concentration in the vehicle.

The test item preparation was made freshly on the morning of administration by the CIT Pharmacy and any unused material was discarded that same day.

2.2 TEST SYSTEM

2.2.1 Animals

Species, strain and sex: nulliparous and non-pregnant female rat, Sprague-Dawley Rj: SD (IOPS Han).
Reason for this choice: rodent species generally accepted by regulatory authorities for this type of study.
Breeder: Janvier, Le Genest-Saint-Isle, France.
Number and sex: 3 groups of three females were used.
Age/weight: on the day of treatment, the animals were approximately 8 weeks old, and had a mean body weight ± standard deviation of 189 ± 6 g.
Acclimation: at least 5 days before the beginning of the study.
Allocation to study: before the beginning of the study, on day 1, the required number of animals was selected according to body weight and clinical condition.
Identification: individually by earnotches.

2.2.2 Environmental conditions

The conditions in the animal room were set as follows:
- temperature: 22 ± 2°C
- relative humidity: 30 to 70%
- light/dark cycle: 12 h/12 h
- ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity were under continuous control and recording. The records were checked daily and filed. In addition to these daily checks, the housing conditions and corresponding instrumentation and equipment are verified and calibrated at regular intervals.
The animals were housed in polycarbonate cages with stainless steel lid (48 cm x 27 cm x 20 cm). Each cage contained one to seven animals during the acclimation period and three rats of the same group during the treatment period.
Each cage contained autoclaved sawdust (SICSA, Alfortville, France).
Sawdust is analyzed by the supplier for composition and contaminant levels.

2.2.3 Food and water

All the animals had free access to SsniffR/M-H pelleted diet (SSNIFF Spezialdiäten GmbH, Soest, Germany), except as noted in "2.3.1 Fasting of the animals".
Each batch of food is analyzed by the supplier for composition and contaminant levels.
The diet formula is presented in appendix 2.

Drinking water filtered by a FG Millipore membrane (0.22 micron) was provided *ad libitum*.
Bacteriological and chemical analyses of water are performed regularly by external laboratories.

These analyses include the detection of possible contaminants (pesticides, heavy metals and nitrosamines).

No contaminants were known to have been present in the diet, drinking water or bedding material at levels which may be expected to have interfered with or prejudiced the outcome of the study.

2.3 TREATMENT

2.3.1 Fasting of the animals

The animals were fasted for an overnight period of approximately 18 hours before dosing, but had free access to water.
Food was given back approximately 4 hours after administration of the test item (dose-level of 300 mg/kg) or after the first administration of the test item (dose-level of 2000 mg/kg).

2.3.2 Study design

Three females were used for each step.
The dose-level used as the starting dose-level was selected from one of four fixed levels, 5, 50, 300 or 2000 mg/kg body weight.

As no information on the toxic potential of the test item was available, for animal welfare reasons, the starting dose-level of 300 mg/kg was chosen.

After the first assay, as no deaths occurred, another assay was carried out on three animals at the next higher dose-level, *i.e.* 2000 mg/kg.
After the second assay, as no deaths occurred, the results were then confirmed in three other females at the dose-level of 2000 mg/kg.

The study design was as follows:

Dose-level (mg/kg)	Volume (mL/kg)	Female
300	10	3
2000	14.3	3
2000	14.3	3

2.3.3 Administration of the test item

The dosage form preparations were administered to the animals under a volume of 10 mL/kg (dose-level of 300 mg/kg) or 14.3 mL/kg (dose-level of 2000 mg/kg).

The administration was performed once (dose-level of 300 mg/kg) or twice at a 2-hour interval (dose-level of 2000 mg/kg) by oral route using a metal gavage tube fitted to a 2 or 5 mL plastic syringe (0.1 or 0.2 mL graduations).

The volume administered to each animal was adjusted according to body weight determined on the day of treatment.

2.4 CLINICAL EXAMINATIONS

The administration was performed in the morning of day 1; it was followed by a 14-day observation period.

2.4.1 Clinical signs and mortality

The animals were observed frequently during the hours following administration of the test item, for detection of possible treatment-related clinical signs. Thereafter, observation of the animals was made at least once a day.
Type, time of onset and duration of clinical signs were recorded for each animal individually.

2.4.2 Body weight

The animals were weighed individually just before administration of the test item on day 1 and then on days 8 and 15.

The body weight gain of the treated animals was compared to that of CIT control animals with the same initial body weight.

2.5 PATHOLOGY

2.5.1 Sacrifice

On day 15, all animals were killed by carbon dioxide asphyxiation.

2.5.2 Macroscopic necropsy examination

All study animals were subjected to a macroscopic examination as soon as possible after death. After opening the thoracic and abdominal cavities, a macroscopic examination of the main organs (digestive tract, heart, kidneys, liver, lungs, pancreas, spleen and any other organs with obvious abnormalities) was performed.

2.5.3 Preservation of tissues

No organ samples were taken.

2.6 EVALUATION AND INTERPRETATION OF THE RESULTS

The interpretation of results was based on the flow charts of Annex 2 of the OECD Guideline No. 423, 17th December 2001 and of Annex 3 of the Directive 2004/73/EC, B.1 tris, 29th April 2004.

2.7 ARCHIVING

The following study materials are archived by CIT, 27005 Evreux, France, for 10 years after the end of the *in vivo* phase of the study:

- Study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments.

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost). The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.
In addition, raw data not specific to the study including, but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration, are also archived by CIT for at least 30 years.

2.8 CHRONOLOGY OF THE STUDY

The chronology of the study was as follows:

Procedure	Date
Experimental starting date (first treatment)	07 August 2007
Experimental completion date (necropsy of the last animal)	11 September 2007

2.9 STUDY PLAN ADHERENCE

The study was performed in accordance with [redacted] subsequent amendments, with the following deviations from the agreed Study plan:

- the temperature and relative humidity recorded in the animal room were sometimes outside of the target ranges specified in the Study plan,
- on day 1, the body weight of one animal (female No. 01) was slightly lower than 180 g (177 g),
- the actual administered dose was 2000 mg/kg (instead of 2002 mg/kg as specified in the amendment to the Study plan).

These minor deviations were not considered to have compromised the validity or integrity of the study.

3. RESULTS

3.1 CLINICAL EXAMINATIONS

3.1.1 Clinical signs and mortality (table 1)

Dose-level of 300 mg/kg (three females)
No deaths and no clinical signs were noted at this dose-level.

Dose-level of 2000 mg/kg (three females then confirmation on three other females)
No deaths occurred.
Hypoactivity, piloerection and dyspnea were noted in 3/6 animals on day 1.

3.1.2 Body weight (figure 1, tables 2 and 3)

When compared to CIT historical control animals, a slightly lower body weight gain was noted between day 1 and day 8 in 1/3 females treated at the dose-level of 300 mg/kg, without any relevant consequence at the end of the observation period, and in 1/6 females treated at the dose-level of 2000 mg/kg, between day 8 and day 15. The body weight gain of the other animals treated at the dose-level of 300 or 2000 mg/kg was not affected by treatment with the test item.

3.2 PATHOLOGY (table 4)

Macroscopic examination of the main organs of the animals revealed no apparent abnormalities.

4. CONCLUSION

Under the experimental conditions of this study, the oral LD_0 of the test item [redacted] 2000 mg/kg in rats.

According to the classification criteria laid down in Council Directive 67/548/EEC (and subsequent adaptations), concerning the potential toxicity by oral route, the test item should not be classified.

Figure 1: Mean body weight of the treated animals

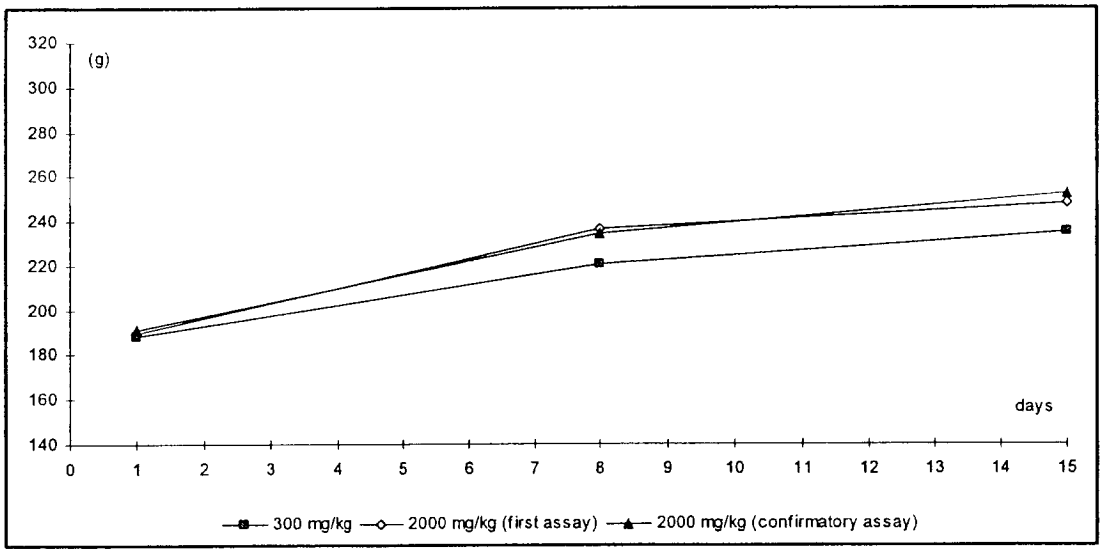


Table 1: Individual clinical signs and mortality

Dose-level (mg/kg)	Time	Females	Mortality	Clinical signs
300	30 min 1 h - 2 h - 4 h D 2 to D 15	01-02-03	No	None
2000 (first assay)	15 min - 1 h - 2 h	04-05-06	No	None
	2 h 30	05-06	No	Hypoactivity, piloerection, dyspnea
		04	No	Piloerection, dyspnea
	4 h - 6 h	04-05-06	No	Hypoactivity, piloerection, dyspnea
	D 2 to D 5	04-05-06	No	None
2000 (confirmatory assay)	30 min -1 h 2 h - 2 h 30 - 4 h D 2 to D 15	07-08-09	No	None

min : minutes
h : hour
D : day

Table 2: Individual and mean body weight and weekly body weight change of treated rats (g)

Dose-level	Volume	Sex	Animals	Days				
mg/kg	mL/kg			1	(1)	8	(1)	15
300	10	Female	01	177	35	212	12	224
			02	195	37	232	13	245
			03	192	26	218	18	236
			M	188	33	221	14	235
			SD	10	6	10	3	11
2000 (first assay)	14.3	Female	04	185	50	235	17	252
			05	193	40	233	15	248
			06	190	51	241	4	245
			M	189	47	236	12	248
			SD	4	6	4	7	4
2000 (confirmatory assay)	14.3	Female	07	190	41	231	22	253
			08	186	46	232	21	253
			09	197	44	241	9	250
			M	191	44	235	17	252
			SD	6	3	6	7	2

(1) = body weight gain
M = mean
SD = standard deviation

Table 3: Body weight - CIT historical data of control animals dosed by oral route

Check of the body weight (g) of CIT historical control animals

Method : Acute oral administration

CIT Studies / Experimental Completion date : CIT/Study Nos. 27218 RDR / February 2004
29691 RDR / April 2005
31103 RDR / January 2006

Reference item : Purified water
Volume of administration : 10 mL/kg

Animals
Species, strain : Rat, Sprague-Dawley Rj: SD (IOPS Han)
Breeder : Janvier, Le Genest-Saint-Isle, France
Age on day 1 : 8 weeks

Volume (mL/kg)	Sex		Days 1	(1)	8	(1)	15
10	Female	M	200	38	240	15	257
		SD	8	5	7	6	8
		n	30	30	30	30	30

M : mean
(1) : body weight gain
SD : standard deviation
n : number of animals

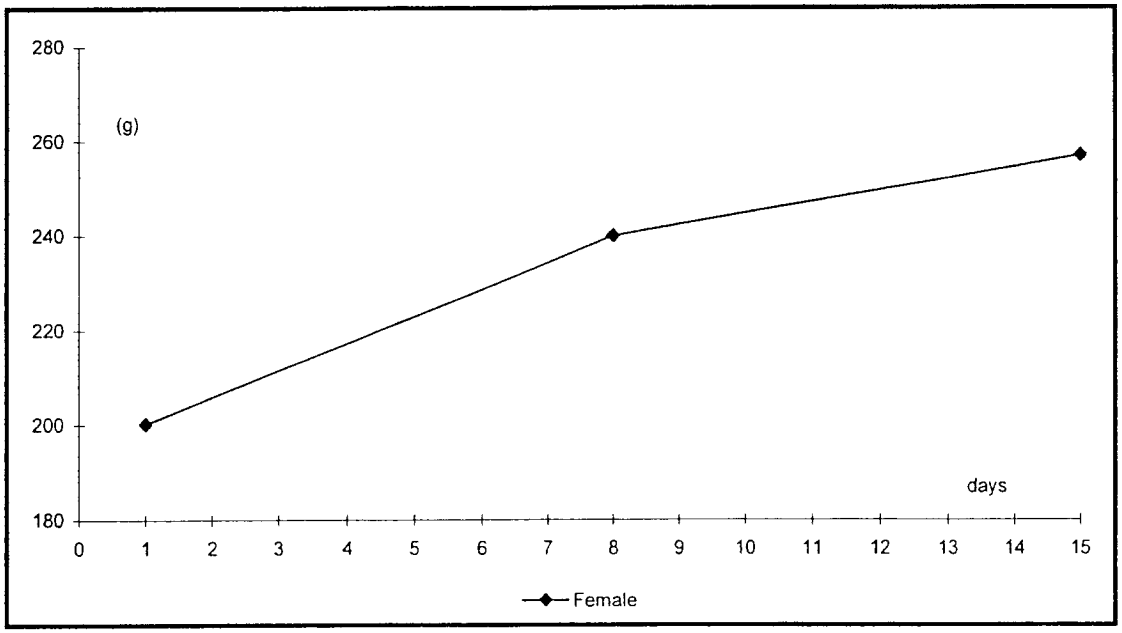


Table 4: Individual macroscopic examinations at necropsy

Dose-level (mg/kg)	Time	Females	Macroscopic abnormalities
300	D 15	01-02-03	No apparent abnormalities
2000	D 15	04-05-06-07-08-09	No apparent abnormalities

D: day

[redacted]

APPENDICES

1. Test article description and analytical certificate

[redacted]

TEST ARTICLE DESCRIPTION

[redacted]

IDENTITY

Test article name	:	[redacted]
Chemical name	:	
CAS number	:	
EINECS number	:	
Origin	:	
Batch number	:	
Arkema filing number	:	

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	black powder
Particule size	:	30 µm (approximately)
Specific Gravity	:	2,1 kg/m3 at 20°C
Autoignition temperature	:	> 400 °C (standard : NF EN 50281-2-1)
Solubility	:	in water : insoluble

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See Safety Data Sheet.

STORAGE AND DISPOSAL

Storage	:	Keep hermetically closed in a dry, cool and well-ventiled place .
Expiry date	:	June 2008
Disposal	:	Incineration

[redacted]

[redacted]

[redacted]

DETERMINATION / *ITEM*	RESULTAT / *RESULT*	**Référence de la méthode d'analyse / *Analysis reference***
Powder characteristics		
Ash content (%)	7.6%	ATG
Apparent density (g/cm³)	70	Weigh-in
[redacted]	[redacted]	[redacted]

Nom du responsable du laboratoire/ *Laboratory Director* :

Signature

[redacted]

2. Diet formula

[redacted]

SsniffR/M-H

Complete diet for rats/mice - maintenance

Crude proteins	19.00 %
Crude fat	3.30 %
Crude fiber	4.90 %
Crude ash	6.70 %

Constituents

Calcium	1.00 %
Phosphorus	0.70 %
Sodium	0.25 %
Magnesium	0.20 %
Potassium	0.90 %

Amino Acids

Lysine	1.00 %
Methionine	0.30 %
Cystine	0.30 %
Glycine	0.90 %
Leucine	1.30 %
Isoleucine	0.70 %
Arginine	1.20 %
Phenylalanine	0.90 %
Tryptophan	0.25 %
Histidine	0.50 %
Tyrosine	0.60 %
Aspartic acid	1.70 %
Glutaminic acid	3.80 %
Valine	0.90 %
Threonine	0.70 %

Vitamins (je kg)

A	15,000 IE
D3	1,000 IE
E	100 mg
B1	10 mg
B2	20 mg
B6	12 mg
B12	80 µg
Biotin	400 µg
Pantothenic acid	30 mg
Choline	1,600 mg
Folic acid	4 mg
Nicotic acid	60 mg
K3	5 mg
Inositol	50 mg

Trace elements (je kg)

Manganese	90 mg
Copper	12 mg
Zinc	75 mg
Iodine	2 mg
Iron	220 mg
Selenium	0.2 mg
Cobalt	2 mg

ME (je kg) **12.2 MJ**

Item numbers

V1530 Meal
V1531 Micromeal
V1534 Pellets 10 mm
V1535 Pellets 15 mm

3. CIT GLP certificate

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

Paris, le - 9 JUIL. 2007

Objet : Evaluation de la conformité aux Bonnes Pratiques de Laboratoires (BPL) selon les directives 2004/9/CE et 2004/10/CE du 11 février 2004.

***Subject** : Assessment of compliance with Good Laboratory Practices (GLP) under the EC directives 2004/9 and 2004/10 of 11 February 2004.*

Consécutivement à votre engagement vis-à-vis du GIPC et du COFRAC et en application du décret n° 2006-1523 du 4 décembre 2006 concernant les bonnes pratiques de laboratoires et modifiant le décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Laboratoires a décidé pour votre installation du statut suivant :

Following your engagement vis-à-vis the GIPC and COFRAC and in application of the decree n° 2006-1523 of 4 December 2006 relating to the good laboratory practices and modifying the decree n° 81-278 of 25 March 1981 giving birth to an interministerial group of chemical products (GIPC), I confirm to you that the GIPC, given the results of the inspection realised by the French Committee of accreditation (COFRAC) – Laboratory Section has taken the following decision relating to your installation:

Respect des principes de BPL
Respect of the GLP principles

Domaines de reconnaissance:
1 - essais physico-chimiques
2 - études de toxicité
3 - études de mutagénicité
4 - études écotoxicologiques sur les organismes aquatiques et terrestres
8 - méthodes de chimie analytique et clinique

Areas of expertise :
1 = Physico-chemical testing
2 = Toxicity studies
3 = Mutagenicity studies
4 = Environmental toxicity studies on aquatic or terrestrial organisms
8 = Analytical and clinical chemistry

Date d'inspection : 7-8 mars 2007
Date of inspection : 7-8 mars 2007

Inspection de renouvellement (i.r)
Renewal inspection (i.r)

Date de décision du GIPC : 29 juin 2007
Date of GIPC decision: 29 juin 2007

Date de prise d'effet : 8 mars 2007
Date of implementation: 8 mars 2007

Année de première conformité : 1989
Year of the first conformity: 1989

Durée de validité: 18 mois
Time of validity: 18 months

Le Président,

Pierre CREYSSEL
Conseiller d'Etat h

CENTRE INTERNATIONAL DE TOXICOLOGIE
(CIT)
MISEREY – BP 563
27005 EVREUX CEDEX

CONFIDENTIAL

CIT
Safety & Health
Research Laboratories

SPONSOR

[redacted]

TEST ITEM

[redacted]

STUDY TITLE

ACUTE DERMAL TOXICITY IN RATS

STUDY DIRECTOR

Catherine Pelcot

DATE OF ISSUE

15 April 2008

TEST FACILITY

CIT
BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER

[redacted]

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with CIT's standard operating procedures and the following principles of Good Laboratory Practice:

- OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents.
- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20.2.2004).
- Décret N° 2006-1523 du 04 décembre 2006 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 06 décembre 2006), Ministère de l'Economie, des Finances et de l'Industrie.

The study was also conducted in compliance with the following Animal Protection regulations:

- Council Directive 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.
- Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation, OECD Environmental Health and Safety Publications, No. 19.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at CIT, BP 563, 27005 Evreux, France.

Toxicology

C. Pelcot
Study Director

Study completion date: 31 March 2008

[redacted]

OTHER CIT SCIENTIST INVOLVED IN THE STUDY

Director of Toxicology
CIT Management

J.J. Legrand Date: 02 April 2008
Doctor of Veterinary Medicine

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT:

The CIT Quality Assurance Unit conducted the inspections detailed below:

Type of inspection	Dates		
	Inspection	Reported to the Study Director	Reported to Management
Study plan	27 July 2007	27 July 2007	02 August 2007
Report	13 February 2008	14 February 2008	12 March 2008

In addition, at about the same time, process-based and facility inspections relevant to this study were carried out by the Quality Assurance Unit.

The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

A. DE CECCO
CIT Quality Assurance Unit

Date: 15 Apr 2008

[redacted]

SUMMARY

[redacted]

OECD (No. 402, 24th February 1987) and EC (92/69/EEC, B.3, 31st July 1992) guidelines.
The study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

The test item was applied to the skin of one group of ten Sprague-Dawley rats (five males and five females).

The application was performed with the test item in its original form at the dose-level of 2000 mg/kg.
The test site was then covered by a semi-occlusive dressing for 24 hours.

Clinical signs, mortality and body weight gain were checked for a period of 14 days following the single application of the test item.

All animals were subjected to necropsy.

Results

No deaths and no clinical signs were observed during the study.
A black coloration of the skin was noted in all the animals from day 2 until day 10 and in all the males and in one female between day 11 and day 15 (end of the observation period). This coloration masked the evaluation of cutaneous reactions in all the animals from day 2 until day 6.
Crusts were observed in 1/5 males and 2/5 females between day 11 and day 15 (end of the observation period).

When compared to CIT historical control animals, the overall body weight gain of the animals was not affected by treatment with the test item.

No apparent abnormalities were observed at necropsy in any animal.

Conclusion

Under the experimental conditions of this study, the dermal LD_0 of the test item [redacted] 2000 mg/kg in rats.

According to the classification criteria laid down in Council Directive 67/548/EEC (and subsequent adaptations), concerning the potential toxicity by dermal route, the test item should not be classified.

RESUME

[redacted]
conformément aux lignes directrices de l'OCDE (n° 402, 24 février 1987) et de la CEE (92/69/CEE, B.3, 31 juillet 1992).
L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthode

Le produit a été appliqué sur la peau d'un groupe de 10 rats Sprague-Dawley (5 mâles et 5 femelles).

L'application a été effectuée avec le produit tel quel à la dose de 2000 mg/kg.
Le site de traitement a ensuite été recouvert d'un pansement semi-occlusif pendant 24 heures.

Les signes cliniques, la mortalité et l'évolution pondérale des animaux ont été suivis pendant une période de 14 jours après l'application unique du produit.

Un examen anatomopathologique a été effectué sur tous les animaux.

Résultats

Aucun signe clinique ni aucune mortalité ne sont observés pendant l'étude.
Une coloration noire de la peau est notée chez tous les animaux du Jour 2 au Jour 10 et chez tous les mâles et 1 femelle entre le Jour 11 et le Jour 15 (fin de la période d'observation). Cette coloration a masqué l'évaluation des réactions cutanées chez tous les animaux du Jour 2 au Jour 6.
Des croûtes sont observées chez 1/5 mâle et 2/5 femelles entre le Jour 11 et le Jour 15 (fin de la période d'observation).

Comparée à celle des animaux témoins historiques du CIT, l'évolution pondérale des animaux n'est pas influencée par le traitement.

L'examen macroscopique des principaux organes des animaux ne met en évidence aucune anomalie apparente.

Conclusion

[redacted]
le rat.

Selon les critères de classification décrits dans la Directive 67/548/CEE (et ses adaptations) concernant la toxicité aiguë par voie dermale, le produit ne devrait pas être classé.

1. INTRODUCTION

The objective of this study was to evaluate the toxicity of the test item GRAPHISTRENGTH C100 micronised following a single dermal application to rats.

In the assessment of the toxic characteristics of a test item, determination of acute dermal toxicity is an initial step. It provides information on health hazards likely to arise following a short-term exposure by the dermal route in humans.

The study was conducted in compliance with:
- OECD guideline No. 402, 24th February 1987,
- EC Directive No. 92/69/EEC, B.3, 31st July 1992.

2. MATERIALS AND METHODS

2.1 TEST ITEM

2.1.1 Identification

- supplier: [redacted]
- name: [redacted]
- batch number: [redacted]
- CAS number: [redacted]
- Description at receipt: [redacted] powder
- container: one plastic flask
- date of receipt: 29 June 2007
- storage conditions: at room temperature and protected from humidity
- composition: see analytical certificate
- expiry date: June 2008.

Data relating to the characterization of the test item are documented in a test article description and in an analytical certificate (presented in appendix 1) provided by the Sponsor.

2.1.2 Dosage form preparation

The test item was administered in its original form.

2.1.3 Other item

Purified water (prepared at CIT by reverse osmosis) was used in order to moisten the test item and ensure a good contact with the skin.

2.2 TEST SYSTEM

2.2.1 Animals

Species, strain: rat, Sprague-Dawley Rj: SD (IOPS Han).
Reason for this choice: rodent species generally accepted by regulatory authorities for this type of study.
Breeder: Janvier, Le Genest-Saint-Isle, France.
Number and sex: one group of ten animals (five males and five females).
Females were nulliparous and non pregnant.
Age/weight: on the day of treatment, the animals were approximately 8 weeks old and had a mean body weight ± standard deviation of 287 ± 6 g for the males and 214 ± 5 g for the females.
Acclimation: 4 days before the beginning of the study.
Identification: individually by earnotches.

2.2.2 Environmental conditions

The conditions in the animal room were set as follows:
- temperature: 22 ± 2°C
- relative humidity: 30 to 70%
- light/dark cycle: 12 h/12 h
- ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity were under continuous control and recording. The records were checked daily and filed. In addition to these daily checks, the housing conditions and corresponding instrumentation and equipment are verified and calibrated at regular intervals.
During the acclimation period, one to seven animals of the same sex were housed in polycarbonate cages with stainless steel lid (48 cm x 27 cm x 20 cm).
During the treatment period, the animals were housed individually in polycarbonate cages with stainless steel lid (35.5 cm x 23.5 cm x 19.3 cm).
Each cage contained autoclaved sawdust (SICSA, Alfortville, France).
Sawdust is analyzed by the supplier for composition and contaminant levels.

2.2.3 Food and water

All the animals had free access to SsniffR/M-H pelleted diet (SSNIFF Spezialdiäten GmbH, Soest, Germany). Each batch of food is analyzed by the supplier for composition and contaminant levels.
The diet formula is presented in appendix 2.

Drinking water filtered by a FG Millipore membrane (0.22 micron) was provided *ad libitum*.
Bacteriological and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides, heavy metals and nitrosamines).

No contaminants were known to have been present in the diet, drinking water or bedding material at levels which may be expected to have interfered with or prejudiced the outcome of the study.

2.3 TREATMENT

2.3.1 Study design

As the test item was anticipated to be non-toxic at the dose-level of 2000 mg/kg, a limit test was performed by application of 2000 mg/kg of the test item to one group of ten animals (five males and five females).

2.3.2 Preparation of the animals

On the day before treatment, the dorsal area of each animal was clipped (*i.e.* approximately 5 cm x 7 cm for males and 5 cm x 6 cm for females) using an electric clipper. Only animals with healthy intact skin were used for the study.

2.3.3 Administration of the test item

A single dose of 2000 mg/kg of the test item in its original form was placed on a hydrophilic gauze pad (pre-moistened with 2 mL of purified water) and then applied to an area of the skin representing approximately 10% of the total body surface of the animals, calculated according to Meeh's formula (1) (*i.e.* approximately 5 cm x 7 cm for the males and 5 cm x 6 cm for the females). The test item and the gauze pad were held in contact with the skin for 24 hours by means of an adhesive hypoallergenic aerated semi-occlusive dressing and a restraining bandage. This dressing prevented ingestion of the test item by the animal.
On removal of the dressing, any residual test item could not be removed using a moistened cotton pad.

The dose applied to each animal was adjusted according to the body weight determined on the day of treatment.

2.4 CLINICAL EXAMINATIONS

2.4.1 Clinical signs and mortality

The animals were observed frequently during the hours following administration of the test item, for detection of possible treatment-related clinical signs. Thereafter, observation of the animals was made at least once a day until day 15.
Type, time of onset and duration of clinical signs were recorded for each animal individually.

From day 2, any local cutaneous reaction was recorded.

2.4.2 Body weight

The animals were weighed individually just before administration of the test item on day 1 and then on days 8 and 15.

The body weight gain of the treated animals was compared to that of CIT control animals with a similar initial body weight.

---

(1) Meeh's formula

$$S = k\sqrt[3]{p^2}$$

S = total surface of the animal in dm^2
p = weight of the animal in grams
k = 0.09 for the rat

2.5 PATHOLOGY

2.5.1 Sacrifice

On day 15, all animals were killed by carbon dioxide asphyxiation.

2.5.2 Macroscopic necropsy examination

All study animals were subjected to a macroscopic examination as soon as possible after death. After opening the thoracic and abdominal cavities, a macroscopic examination of the main organs (digestive tract, heart, kidneys, liver, lungs, pancreas, spleen and any other organs with obvious abnormalities) was performed.

2.5.3 Preservation of tissues

No organ samples were taken.

2.6 DATA EVALUATION

Evaluation of the toxicity of the test item following a single dermal application in rats should include the relationship, if any, between the animals' exposure to the test item and the incidence and severity of all abnormalities including behavioural and clinical abnormalities, macroscopic lesions, body weight changes, mortality and any other toxic effects.

2.7 ARCHIVING

The following study materials are archived by CIT, 27005 Evreux, France, for 10 years after the end of the *in vivo* phase of the study:

- Study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments.

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost). The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.
In addition, raw data not specific to the study including, but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration, are also archived by CIT for at least 30 years.

2.8 CHRONOLOGY OF THE STUDY

The chronology of the study was as follows:

Procedure	Date
Experimental starting date (treatment)	21 August 2007
Experimental completion date (necropsy of the last animal)	04 September 2007

2.9 STUDY PLAN ADHERENCE

The study was performed in accordance with Study plan [redacted] subsequent amendments, with the following deviations from the agreed Study plan:

- the temperature and relative humidity recorded in the animal room were sometimes outside of the target ranges specified in the Study plan,
- the acclimation of the animals was 4 days (instead of at least 5 days) before the beginning of the study.

These minor deviations were not considered to have compromised the validity or integrity of the study.

3. RESULTS

3.1 CLINICAL EXAMINATIONS

3.1.1 Mortality (table 1)

No deaths occurred during the study.

3.1.2 Clinical signs and cutaneous reactions (tables 1 and 2)

No clinical signs were observed during the study.
A black coloration of the skin was noted in all the animals from day 2 until day 10 and in all the males and in one female between day 11 and day 15 (end of the observation period). This coloration masked the evaluation of cutaneous reactions in all the animals from day 2 until day 6.
Crusts were observed in 1/5 males and 2/5 females between day 11 and day 15 (end of the observation period).

3.1.3 Body weight (figure 1, tables 3 and 4)

When compared to CIT historical control animals, the overall body weight gain of the animals was not affected by treatment with the test item.

3.2 PATHOLOGY (table 5)

Macroscopic examination of the main organs of the animals revealed no apparent abnormalities.

4. CONCLUSION

Under the experimental conditions of this study, the dermal LD_0 of the test item [redacted] 2000 mg/kg in rats.

Figure 1: Mean body weight of treated rats

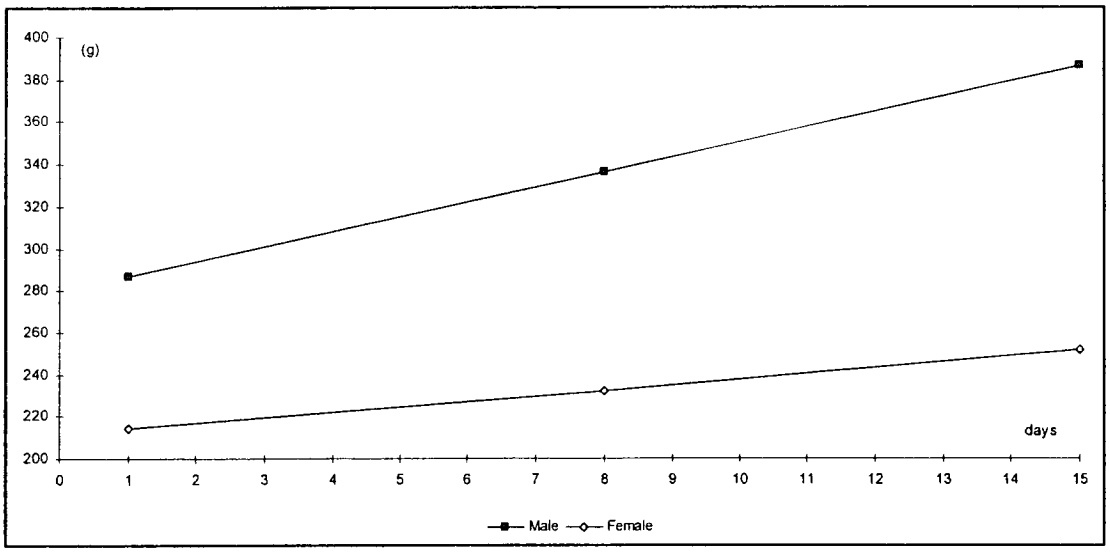


Table 1: Individual clinical signs and mortality

Dose-level (mg/kg)	Time	Animals		Mortality	Clinical signs
		Males	Females		
2000	30 min 2 h - 5 h D 2 to D 15	01-02-03-04-05	06-07-08-09-10	No	None

min : minutes
h : hour
D : day

Table 2: Cutaneous reactions

Dose-level (mg/kg)	Time	Animals		Cutaneous reactions
		Males	Females	
2000	D 2 to D 6	01-02-03-04-05	06-07-08-09-10	Black coloration of the skin which could have masked a possible erythema
	D 7 to D 10	01-02-03-04-05	06-07-08-09-10	Black coloration of the skin No cutaneous reactions
	D 11		06-10	Crusts
		01-02-03-04-05	07	Black coloration of the skin No cutaneous reactions
			08-09	None
	D 12 and D 13	03		Crusts, black coloration of the skin
			06-10	Crusts
		01-02-03-04-05	07	Black coloration of the skin No cutaneous reactions
			08-09	None
	D 14	01-02-03-05	07	Black coloration of the skin No cutaneous reactions
			06-10	Crusts
		04	08-09	None
	D 15	01-02-03-05	07	Black coloration of the skin No cutaneous reactions
			06	Crusts
		04	08-09-10	None

D: day

Table 3: Individual and mean body weight and weekly body weight change (g)

Dose-level mg/kg	Sex	Animals	Days 1	(1)	8	(1)	15
2000	Male	01	295	52	347	53	400
		02	280	49	329	44	373
		03	287	47	334	53	387
		04	288	50	338	49	387
		05	284	50	334	51	385
		M	287	50	336	50	386
		SD	6	2	7	4	10
2000	Female	06	214	17	231	19	250
		07	220	16	236	21	257
		08	206	19	225	20	245
		09	214	15	229	14	243
		10	218	19	237	26	263
		M	214	17	232	20	252
		SD	5	2	5	4	8

(1) = body weight gain
M = mean
SD = standard deviation

Table 4: Body weight - CIT historical data of control animals dosed by dermal route

Check of the body weight (g) of CIT historical control animals

Method : Acute dermal administration

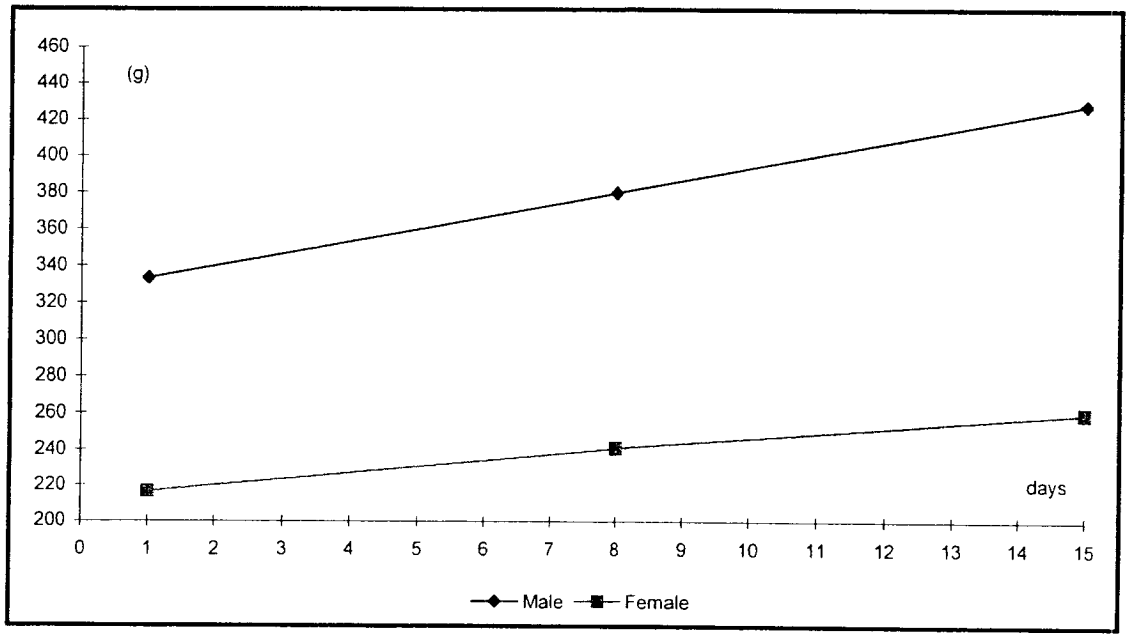
CIT Studies / Experimental Completion date : CIT/Study Nos. 27220 RDR / February 2004
29692 RDR / April 2005
31105 RDR / January 2006

Reference item : Purified water
Volume of administration : 5 mL/kg

Animals
Species, strain : Rat, Sprague-Dawley Rj: SD (IOPS Han)
Breeder : Janvier, Le Genest-Saint-Isle, France
Age on day 1 : 8 weeks

Volume (mL/kg)	Sex		Days				
			1	(1)	8	(1)	15
5	Male	M	333	46	380	48	428
		SD	36	14	32	9	34
		n	29	29	29	29	29
5	Female	M	216	24	241	19	260
		SD	9	11	14	9	16
		n	29	29	29	29	29

M : mean
(1) : body weight gain
SD : standard deviation
n : number of animals



[redacted] 20

Table 5: Individual macroscopic examinations at necropsy

Dose-level (mg/kg)	Time	Animals		Macroscopic abnormalities
		Males	Females	
2000	D 15	01-02-03-04-05	06-07-08-09-10	No apparent abnormalities

D: day

[redacted] 21

APPENDICES

[redacted]

1. Test article description and analytical certificate

[redacted]

TEST ARTICLE DESCRIPTION

[redacted]

IDENTITY

Test article name
Chemical name
CAS number
EINECS number
Origin
Batch number
Arkema filing number

[redacted]

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	black powder
Particule size	:	30 µm (approximately)
Specific Gravity	:	2,1 kg/m3 at 20°C
Autoignition temperature	:	> 400 °C (standard : NF EN 50281-2-1)
Solubility	:	in water : insoluble

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See Safety Data Sheet.

STORAGE AND DISPOSAL

Storage	:	Keep hermetically closed in a dry, cool and well-ventiled place .
Expiry date	:	June 2008
Disposal	:	Incineration

[redacted]

24

[redacted]

DETERMINATION / *ITEM*	RESULTAT / *RESULT*	Référence de la méthode d'analyse / *Analysis reference*
Powder characteristics		
Ash content (%)	7.6%	ATG
Apparent density (kg/m^3)	70	Weigh-in
[redacted]	[redacted]	[redacted]

Nom du responsable du laboratoire/ *Laboratory Director* :

Signature

[redacted]

[redacted]

25

2. Diet formula

SsniffR/M-H

Complete diet for rats/mice - maintenance

Crude proteins	19.00 %
Crude fat	3.30 %
Crude fiber	4.90 %
Crude ash	6.70 %

Constituents

Calcium	1.00 %
Phosphorus	0.70 %
Sodium	0.25 %
Magnesium	0.20 %
Potassium	0.90 %

Amino Acids

Lysine	1.00 %
Methionine	0.30 %
Cystine	0.30 %
Glycine	0.90 %
Leucine	1.30 %
Isoleucine	0.70 %
Arginine	1.20 %
Phenylalanine	0.90 %
Tryptophan	0.25 %
Histidine	0.50 %
Tyrosine	0.60 %
Aspartic acid	1.70 %
Glutaminic acid	3.80 %
Valine	0.90 %
Threonine	0.70 %

Vitamins (je kg)

A	15,000 IE
D3	1,000 IE
E	100 mg
B1	10 mg
B2	20 mg
B6	12 mg
B12	80 µg
Biotin	400 µg
Pantothenic acid	30 mg
Choline	1,600 mg
Folic acid	4 mg
Nicotic acid	60 mg
K3	5 mg
Inositol	50 mg

Trace elements (je kg)

Manganese	90 mg
Copper	12 mg
Zinc	75 mg
Iodine	2 mg
Iron	220 mg
Selenium	0.2 mg
Cobalt	2 mg

ME (je kg) **12.2 MJ**

Item numbers

V1530 Meal
V1531 Micromeal
V1534 Pellets 10 mm
V1535 Pellets 15 mm

[redacted] 27

3. CIT GLP certificate

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

Paris, le - 9 JUIL. 2007

Objet : Evaluation de la conformité aux Bonnes Pratiques de Laboratoires (BPL) selon les directives 2004/9/CE et 2004/10/CE du 11 février 2004.

***Subject** : Assessment of compliance with Good Laboratory Practices (GLP) under the EC directives 2004/9 and 2004/10 of 11 February 2004.*

Consécutivement à votre engagement vis-à-vis du GIPC et du COFRAC et en application du décret n° 2006-1523 du 4 décembre 2006 concernant les bonnes pratiques de laboratoires et modifiant le décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Laboratoires a décidé pour votre installation du statut suivant :
Following your engagement vis-à-vis the GIPC and COFRAC and in application of the decree n° 2006-1523 of 4 December 2006 relating to the good laboratory practices and modifying the decree n° 81-278 of 25 March 1981 giving birth to an interministerial group of chemical products (GIPC), I confirm to you that the GIPC, given the results of the inspection realised by the French Committee of accreditation (COFRAC) – Laboratory Section has taken the following decision relating to your installation.

Respect des principes de BPL
Respect of the GLP principles

Domaines de reconnaissance:
1 - essais physico-chimiques
2 - études de toxicité
3 - études de mutagénicité
4 - études écotoxicologiques sur les organismes aquatiques et terrestres
8 - méthodes de chimie analytique et clinique

Areas of expertise :
1 = Physico-chemical testing
2 = Toxicity studies
3 = Mutagenicity studies
4 = Environmental toxicity studies on aquatic or terrestrial organisms
8 = Analytical and clinical chemistry

Date d'inspection : 7-8 mars 2007
Date of inspection : 7-8 mars 2007

Inspection de renouvellement (i.r)
Renewal inspection (i.r)

Date de décision du GIPC : 29 juin 2007
Date of GIPC decision: 29 juin 2007

Date de prise d'effet : 8 mars 2007
Date of implementation: 8 mars 2007

Année de première conformité : 1989
Year of the first conformity: 1989

Durée de validité: 18 mois
Time of validity: 18 months

Le Président,

Pierre CREYSSEL
Conseiller d'Etat h

CENTRE INTERNATIONAL DE TOXICOLOGIE
(CIT)
MISEREY – BP 563
27005 EVREUX CEDEX

CIT
Safety & Health
Research Laboratories

SPONSOR

[redacted]

TEST ITEM

[redacted]

STUDY TITLE
ACUTE EYE IRRITATION IN RABBITS

STUDY DIRECTOR
Catherine Pelcot

DATE OF ISSUE
25 April 2008

TEST FACILITY
CIT
BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER
[redacted]

IFM Recherche
S N C au Capital de 846 092 €
788 060 465 R C.S Evreux
VAT FR19 788 060 465
Agrément Crédit Impôt Recherche

B.P. 563 27005 Evreux Cedex France
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E-mail CIT@citox.com
Web site www.citox.com

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with the principles of Good Laboratory Practice as described in:

- OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents.
- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20.2.2004).
- Décret N° 2006-1523 du 04 décembre 2006 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 06 décembre 2006), Ministère de l'Economie, des Finances et de l'Industrie.

The study was also conducted in compliance with the following Animal Protection regulations:

- Council Directive 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.
- Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation, OECD Environmental Health and Safety Publications, No. 19.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at CIT, BP 563, 27005 Evreux, France.

Toxicology

C. Pelcot
Study Director

Study completion date: 22 April 2008

OTHER CIT SCIENTIST INVOLVED IN THE STUDY

Director of Toxicology
CIT Management

J.J. Legrand Date: 25 April 2008
Doctor of Veterinary Medicine

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT:

The CIT Quality Assurance Unit conducted the inspections detailed below:

Type of inspection	Dates		
	Inspection	Reported to the Study Director	Reported to Management
Study plan	27 July 2007	27 July 2007	02 August 2007
Report	25 March 2008	27 March 2008	08 April 2008

In addition, at about the same time, process-based and facility inspections relevant to this study were carried out by the Quality Assurance Unit.

The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

A. DE CECCO
CIT Quality Assurance Unit

Date: 25 Apr 2008

[redacted]

SUMMARY

[redacted]

evaluated in rabbits according to OECD (no. 405, 24th April 2002) and EC (2004/73/EC, B.5, 29th April 2004) guidelines.
The study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

The test item was first administered to a single male New Zealand White rabbit. Since the test item was irritant on this first animal, but without persistence until the end of the observation period, it was then evaluated sequentially in two other animals.

A single dose of the test item in its original form was introduced into the left conjunctival sac. The right eye was not treated and served as control.
The eyes were not rinsed after administration of the test item.

Ocular reactions were observed approximately 1 hour, 24, 48 and 72 hours after the administration and then daily until complete reversibility of the ocular reactions (day 9 at the latest).

The mean values of the scores for chemosis, redness of the conjunctiva, iris lesions and corneal opacity were calculated for each animal.

Results

A slight to marked chemosis was noted in all the animals from day 1 until day 7 (1/3 animals) or 8 (2/3 animals). A slight to severe redness of the conjunctiva was observed in all the animals from day 1 until day 5 (1/3 animals) or 8 (2/3 animals). A clear discharge was observed in all the animals from day 1 until day 2, 5 or 6.
An iritis was noted in all the animals on day 2; it persisted in one animal until day 4.
A slight or moderate corneal opacity was recorded in all the animals on days 2 and 3; it persisted until day 5 in 2/3 animals. This corneal opacity covered the whole area of the cornea of 1/3 animals on day 2.

Mean scores calculated for each animal over 24, 48 and 72 hours were 2.7, 2.3 and 2.7 for chemosis, 2.0, 1.7 and 2.7 for redness of the conjunctiva, 0.3, 0.3 and 1.3 for iris lesions and 2.0, 1.0 and 2.0 for corneal opacity.

Conclusion

[redacted]

According to the classification criteria laid down in Council Directive 67/548/EEC (and subsequent adaptations), the test item should be considered as irritant to eyes.

[redacted]

RESUME

[redacted]

le Lapin ont été évaluées selon les lignes directrices de l'OCDE (n° 405, 24 février 1987) et de la CEE (92/69/CEE, B.5, 31 juillet 1992).
L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthode

Le produit a d'abord été appliqué sur un seul Lapin mâle New Zealand White. Le produit ayant montré des propriétés irritantes sur ce premier animal mais sans persistance jusqu'à la fin de la période d'observation, il a ensuite été testé séquentiellement sur deux autres animaux.

Une dose unique de produit tel quel a été introduite dans le cul-de-sac conjonctival de l'oeil gauche. L'oeil droit a servi de témoin.
Aucun rinçage des yeux n'a été réalisé après l'administration du produit.

Les réactions oculaires ont été observées environ 1, 24, 48 et 72 heures après l'administration puis quotidiennement jusqu'à réversibilité complète des lésions oculaires observées (jour 9 au plus tard).

La moyenne des scores pour le chémosis, la rougeur de la conjonctive, les lésions de l'iris et l'opacité de la cornée a été calculée pour chaque animal.

Résultats

Un chémosis léger à marqué est noté chez tous les animaux du jour 1 aux jours 7 (1/3 animal) ou 8 (2/3 animaux). Une rougeur de la conjonctive légère à grave est observée chez tous les animaux du jour 1 aux jours 5 (1/3 animal) ou 8 (2/3 animaux). Un larmoiement clair est observé chez tous les animaux du jour 1 aux jours 2, 5 ou 6.
Une inflammation de l'iris est notée chez tous les animaux au jour 2 ; elle persiste chez 1 animal jusqu'au jour 4.
Une opacité cornéenne légère ou modérée est observée chez tous les animaux aux jours 2 et 3 ; elle persiste jusqu'au jour 5 chez 2/3 animaux. Cette opacité cornéenne a couvert la totalité de la cornée d'1/3 animal au jour 2.

La moyenne des scores enregistrés pour chaque animal après 24, 48 et 72 heures est de 2,7 ; 2,3 et 2,7 pour le chémosis, 2,0 ; 1,7 et 2,7 pour la rougeur de la conjonctive, 0,3 ; 0,3 et 1,3 pour les lésions de l'iris et 2,0 ; 1,0 et 2,0 pour l'opacité cornéenne.

Conclusion

[redacted]

Selon les critères de classification décrits dans la Directive 67/548/CEE (et ses adaptations), le produit est considéré comme irritant pour les yeux.

1. INTRODUCTION

[redacted]

In the assessment of the toxic characteristics of a test item, determination of the irritant effects on the eyes of mammals is an important initial step. Information derived from this test serves to indicate the possible hazards likely to arise from exposure of the eyes, and associated mucous membranes, to the test item.

This study was conducted in compliance with:
- OECD guideline No. 405, 24th April 2002,
- EC Directive No. 2004/73/EC, part B.5, 29th April 2004.

2. MATERIALS AND METHODS

2.1 TEST ITEM

2.1.1 Identification

[redacted]

- Description at receipt: black powder
- container: one plastic flask
- date of receipt: 29 June 2007
- storage conditions: at room temperature and protected from humidity
- composition: see analytical certificate
- expiry date: June 2008.

Data relating to the characterization of the test item are documented in a test article description and in an analytical certificate (presented in appendix 1) provided by the Sponsor.

2.1.2 Dosage form preparation

The test item was used in its original form.

The pH of the test item at the concentration of 1% in purified water was not measurable (non soluble and colored test item).

2.2 TEST SYSTEM

2.2.1 Animals

Sex, species, strain: male New Zealand White rabbits.
Reason for this choice: species generally accepted by regulatory authorities for this type of study.
Breeder: Grimaud frères selection S.A.S., La Corbière, Roussay, France
Number: three animals were used, as recommended by the international guidelines.
Age/weight: on the day of treatment, the animals were 2 to 4 months old and had a mean body weight ± standard deviation of 2.9 ± 0.1 kg.
Acclimation: at least 5 days before the beginning of the study.
Identification: individual metal ear tag.

2.2.2 Environmental conditions

The conditions in the animal room were set as follows:
- temperature: 18 ± 3°C
- relative humidity: 30 to 70%
- light/dark cycle: 12 h/12 h
- ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity were under continuous control and recording. The records were checked daily and filed. In addition to these daily checks, the housing conditions and corresponding instrumentation and equipment were verified and calibrated at regular intervals.
The animals were housed individually in Techniplast (64 cm x 63 cm x 30 cm) or Pajon (50 cm x 57 cm x 75 cm) cages.
Each cage was equipped with a food container and a water bottle.

2.2.3 Food and water

During the study, the animals had free access to 110C pelleted diet (SAFE, Villemoisson, Epinay-sur-Orge, France).
Food is analyzed regularly by the supplier for composition and contaminant levels.
The diet formula is presented in appendix 2.

Drinking water filtered by a FG Millipore membrane (0.22 micron) was provided *ad libitum*.
Bacteriological and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides, heavy metals and nitrosamines).

No contaminants were known to have been present in the diet or drinking water at levels which may be expected to have interfered with or prejudiced the outcome of the study.

2.3 TREATMENT

2.3.1 Selection of the animals

Just before treatment, the eyes of each animal were examined in order to check the absence of any signs of ocular irritation, ocular defects or pre-existing corneal injury.

2.3.2 Administration of the test item

The test item was first administered to a single animal (No. 474). Since the test item was irritant, but without persistence at the end of the observation period, on this first animal, it was then evaluated sequentially on other animals (No. 483 then No. 484).

A single dose (the maximal quantity of the test item administrable into the eye was approximately 1/3 of the 100 mg required quantity) of the test item in its original form was introduced into the conjunctival sac of the left eye after gently pulling the lower lid away from the eyeball.

The lower and upper eyelids were held together for about one second to avoid any loss of test item. The right eye, which remained untreated, served as control.

The eyes were not rinsed after administration of the test item.

2.4 OCULAR EXAMINATIONS

2.4.1 Duration of the observation period

The eyes were examined approximately 1 hour, 24, 48 and 72 hours after administration of the test item.
Since there were persistent ocular reactions at 72 hours, the observation period was extended up to their complete reversibility (day 9 at the latest).

2.4.2 Description and evaluation of ocular reactions

Conjunctival reactions, iritis and corneal opacification were evaluated daily for each animal.
For the evaluation of corneal opacification (presence or absence, affected area), the eyes were examined under a UV lamp after instillation of one or two drops of 0.5% sodium fluorescein solution (a clear fluorescence is visible in the areas of opacification). This evaluation was performed on day 2 and repeated thereafter whenever necessary.

Ocular reactions were scored according to the following numerical scale:

<u>Conjunctival lesions and discharge</u>
Chemosis (lids and/or nictitating membranes)
. no swelling 0
. any swelling above normal (includes nictitating membranes) 1
. obvious swelling with partial eversion of lids 2
. swelling with lids about half-closed 3
. swelling with lids more than half-closed 4

Redness (refers to palpebral and bulbar conjunctivae, cornea and iris)
. blood vessels normal 0
. a number of blood vessels definitely hyperemic (injected) 1
. diffuse, crimson colour, individual vessels not easily discernible 2
. diffuse, beefy red 3

Discharge
. absence of discharge 0
. slight discharge (does not include small amounts normally found in inner canthus) 1
. discharge with moistening of lids and hairs adjacent to lids 2
. discharge with moistening of lids and hairs on wide area around the eye 3

Iris lesions
. normal 0
. markedly deepened rugae, congestion, swelling, moderate circum-corneal hyperemia, or injection, any of these or combination of any thereof, iris still reacting to light (sluggish reaction is positive) 1
. no reaction to light, haemorrhage, gross destruction (any or all of these) 2

Corneal lesions
Degree of opacity (area most dense taken for reading)
. no ulceration or opacity 0
. scattered or diffuse areas of opacity (other than slight dulling or normal lustre), details of iris clearly visible 1
. easily discernible translucent area, details of iris slightly obscured 2
. nacreous areas, no details of iris visible, size of pupil barely discernible 3
. opaque cornea, iris not discernible through the opacity 4

Area of opacity
. one quarter (or less) but not zero 1
. greater than one quarter but less than a half 2
. greater than one half but less than three quarters 3
. greater than three quarters up to whole area. 4

Any other lesions observed were noted.

2.5 BODY WEIGHT

Each animal was weighted at the beginning (day of treatment) and at the end of the observation period.

2.6 INTERPRETATION OF RESULTS

The results obtained were evaluated in conjunction with the nature and the reversibility of the scores observed, whilst taking into account all the reactions of the treated animals.

Criteria for irritation
A substance or a preparation is considered irritant for the eyes if, when applied to the eye of the animal, significant or severe ocular lesions are caused within 72 hours after exposure and which persist for 24 hours or more after treatment with the test item.
All the scores at each reading time (24, 48 and 72 hours) and for an effect are used for calculating the respective mean values.

2.7 ARCHIVING

The following study materials are archived by CIT, 27005 Evreux, France, for 10 years after the end of the *in vivo* phase of the study:

- Study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments.

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost). The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.
In addition, raw data not specific to the study including, but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration, are also archived by CIT for at least 30 years.

2.8 CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date
Experimental starting date (day of treatment of the first animal)	14 August 2007
Experimental completion date (end of the observation period)	07 September 2007

2.9 STUDY PLAN ADHERENCE

The study was performed in accordance with [redacted]osequent amendments, with the following deviation from the agreed Study plan:

- the temperature and relative humidity recorded in the animal room were sometimes outside of the target ranges specified in the Study plan.

This minor deviation was not considered to have compromised the validity or integrity of the study.

3. RESULTS

The observations recorded during the study are presented in table 1.
The body weight is presented in table 2.

A slight to marked chemosis (grades 1 to 3) was noted in all the animals from day 1 until day 7 (1/3 animals) or 8 (2/3 animals). A slight to severe redness of the conjunctiva (grades 1 to 3) was observed in all the animals from day 1 until day 5 (1/3 animals) or 8 (2/3 animals). A clear discharge was observed in all the animals from day 1 until day 2, 5 or 6.
An iritis of grade 1 was noted in 2/3 the animals on day 2. In the third animal, an iritis of grade 2 was noted on day 2; an iritis of grade 1 persisted until day 4.
A slight or moderate corneal opacity (grade 1 or 2) was recorded in all the animals on day 2; it persisted until day 3 (1/3 animals) or 5 (2/3 animals). This corneal opacity covered the whole area of the cornea of 1/3 animals on day 2.

Mean scores calculated for each animal over 24, 48 and 72 hours were 2.7, 2.3 and 2.7 for chemosis, 2.0, 1.7 and 2.7 for redness of the conjunctiva, 0.3, 0.3 and 1.3 for iris lesions and 2.0, 1.0 and 2.0 for corneal opacity.

4. DISCUSSION

The grade 2 observed in one animal only on day 2 seems doubtful and not coherent with the grades 1 noted the next days.

5. CONCLUSION

[redacted]

Table 1: Individual ocular examinations and mean values of the scores recorded for each animal (24, 48 and 72 hours)

Rabbit number	Region of eye	Description of ocular reactions	Scores 1h D1	24h D2	48h D3	72h D4	Mean irritation score (1)	Interpretation (+) (-)
474	Conjunctivae	Chemosis	3	3	3	2	2.7	(+)
		Redness	2	2	2	2	2.0	(-)
		Discharge	1	2	0	0	0.7	
	Iris		0	1	0	0	0.3	(-)
	Corneal opacity	Intensity	0	2	2	2	2.0	(+)
		Area	0	4	3	1	2.7	
	Other Fluorescein		Su /	Su U	Su U	Su U		
483	Conjunctivae	Chemosis	3	3	2	2	2.3	(+)
		Redness	2	2	2	1	1.7	(-)
		Discharge	1	2	1	1	1.3	
	Iris		0	1	0	0	0.3	(-)
	Corneal opacity	Intensity	0	2	1	0	1.0	(-)
		Area	0	3	1	0	1.3	
	Other Fluorescein		Su /	Su U	* U	* U		
484	Conjunctivae	Chemosis	3	3	3	2	2.7	(+)
		Redness	2	3	3	2	2.7	(+)
		Discharge	1	1	1	1	1.0	
	Iris		0	2	1	1	1.3	(+)
	Corneal opacity	Intensity	0	2	2	2	2.0	(+)
		Area	0	3	3	2	2.7	
	Other Fluorescein		Su /	Su U	* U	* U		

(1) mean of scores on days 2, 3 and 4
h = hour
D = day
(+) = irritant according to E.E.C. criteria
(-) = non-irritant according to E.E.C. criteria
* = none
U = fluorescein batch Nos. L239 and L653
/ = fluorescein not used
Su = residual test item

Table 1 (continued)

Rabbit number	Region of eye	Description of ocular reactions	Scores				
			D5	D6	D7	D8	D9
474	Conjunctivae	Chemosis	2	2	1	1	0
		Redness	2	2	1	1	0
		Discharge	0	0	0	0	0
	Iris		0	0	0	0	0
	Corneal opacity	Intensity	1	0	0	0	0
		Area	1	0	0	0	0
	Other		*	*	*	*	*
	Fluorescein		U	U	/	/	/
483	Conjunctivae	Chemosis	1	1	1	0	-
		Redness	1	0	0	0	-
		Discharge	1	1	0	0	-
	Iris		0	0	0	0	-
	Corneal opacity	Intensity	0	0	0	0	-
		Area	0	0	0	0	-
	Other		*	*	*	*	-
	Fluorescein		/	/	/	/	-
484	Conjunctivae	Chemosis	2	2	2	1	0
		Redness	1	1	1	1	0
		Discharge	1	0	0	0	0
	Iris		0	0	0	0	0
	Corneal opacity	Intensity	1	0	0	0	0
		Area	1	0	0	0	0
	Other		*	*	*	*	*
	Fluorescein		U	U	/	/	/

D = day
* = none
U = fluorescein batch Nos. L239 and L653
/ = fluorescein not used
- = ocular examination not performed

Table 2: Individual body weight (g)

Sex	Animals	Day of treatment	End of the observation period
Male	474	2778	2993
	483	2780	2914
	484	3015	3140
	M	2858	3016
	SD	136	115

M = mean
SD = standard deviation

[redacted]

APPENDICES

[redacted]

1. Test article description and analytical certificate

[redacted]

TEST ARTICLE DESCRIPTION

[redacted]

IDENTITY

Test article name	: [redacted]
Chemical name	:
CAS number	
EINECS number	:
Origin	:
Batch number	:
Arkema filing number	:

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	black powder
Particule size	:	30 µm (approximately)
Specific Gravity	:	2,1 kg/m3 at 20°C
Autoignition temperature	:	> 400 °C (standard : NF EN 50281-2-1)
Solubility	:	in water : insoluble

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See Safety Data Sheet.

STORAGE AND DISPOSAL

Storage	:	Keep hermetically closed in a dry, cool and well-ventiled place .
Expiry date	:	June 2008
Disposal	:	Incineration

[redacted]

[redacted]

DETERMINATION / *ITEM*	RESULTAT / *RESULT*	Référence de la méthode d'analyse / *Analysis reference*
Powder characteristics		
Ash content (%)	7.6%	ATG
Apparent density (kg/m^3)	70	Weigh-in
[redacted]	[redacted]	[redacted]

Nom du responsable du laboratoire/ *Laboratory Director* :

Signature

[redacted]

[redacted]

2. Diet formula

Ref: 110
COMPLETE DIET
RABBIT BREEDING DIET
Appearance: 3 mm diameter granules
Conditioning: bags of 20 kgs

Daily portion: Rabbits 150 g, water *ad libitum*.

FORMULA %

Cereals	33.8
Grain biproducts and leguminous plants	48
Vegetable protein (soya bean meal, yeast)	14
Vitamin and mineral mixture	4.2

AVERAGE ANALYSIS %

Calorific value (Kcal/kg)	3100
Moisture	10
Proteins	15
Lipids	2.3
Carbohydrates (N.F.E.)	48.2
Fibre	17
Minerals (ash)	7.5

AMINO ACID VALUES
(calculated in mg/kg)

Arginine	11300
Cystine	3400
Lysine	9300
Methionine	2800
Tryptophan	2400
Glycine	8700

FATTY ACID VALUES
(calculated in mg/kg)

Palmitic acid	6400
Palmitoleic acid	0
Stearic acid	600
Oleic acid	6400
Linoleic acid	12100
Linolenic acid	2400

MINERALS (calculated in mg/kg)

	Nat. val.	CMV val.	Total
P	3600	2900	6500
Ca	4200	5800	10000
K	12000	0	12000
Na	400	2000	2400
Mg	2500	100	2600
Mn	50	40	90
Fe	150	150	300
Cu	Traces	15	15
Zn	30	45	75
Co	0.1	1.5	1.6
I	0.1	0	0.1
Cl	300	3000	3300

VITAMINS (calculated per kg)

	Nat. val.	CMV val.	Total
Vitamin A	Traces	10000 IU	10000 IU
Vitamin D3	0 IU	1000 IU	1000 IU
Vitamin B1	5 mg	0 mg	5 mg
Vitamin B2	4 mg	0 mg	4 mg
Vitamin B3	20 mg	0 mg	20 mg
Vitamin B6	1 mg	1 mg	2 mg
Vitamin B12	0 mg	0 mg	0 mg
Vitamin E	15 mg	25 mg	40 mg
Vitamin K3	0 mg	1 mg	1 mg
Vitamin PP	60 mg	5 mg	65 mg
Folic acid	0 mg	0 mg	0 mg
Biotin	0 mg	0 mg	0 mg
Choline	1000 mg	1000 mg	2000 mg

Available under quality "Control Ref.: 110"

SAFE, 7 rue Galliéni, Villemoisson, 91360 Epinay-sur-Orge
Tel: 01.69.04.03.57 - Fax : 01.69.04.81.97
(Ref. Doc. UAR: 2000)

[redacted]

3. CIT GLP certificate

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

Paris, le - 9 JUIL. 2007

Objet : Evaluation de la conformité aux Bonnes Pratiques de Laboratoires (BPL) selon les directives 2004/9/CE et 2004/10/CE du 11 février 2004.

Subject : Assessment of compliance with Good Laboratory Practices (GLP) under the EC directives 2004/9 and 2004/10 of 11 February 2004.

Consécutivement à votre engagement vis-à-vis du GIPC et du COFRAC et en application du décret n° 2006-1523 du 4 décembre 2006 concernant les bonnes pratiques de laboratoires et modifiant le décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Laboratoires a décidé pour votre installation du statut suivant :
Following your engagement vis-à-vis the GIPC and COFRAC and in application of the decree n° 2006-1523 of 4 December 2006 relating to the good laboratory practices and modifying the decree n° 81-278 of 25 March 1981 giving birth to an interministerial group of chemical products (GIPC), I confirm to you that the GIPC, given the results of the inspection realised by the French Committee of accreditation (COFRAC) – Laboratory Section has taken the following decision relating to your installation.

Respect des principes de BPL
Respect of the GLP principles

Domaines de reconnaissance:
1 - essais physico-chimiques
2 - études de toxicité
3 - études de mutagénicité
4 - études écotoxicologiques sur les organismes aquatiques et terrestres
8 - méthodes de chimie analytique et clinique

Areas of expertise :
1 = Physico-chemical testing
2 = Toxicity studies
3 = Mutagenicity studies
4 = Environmental toxicity studies on aquatic or terrestrial organisms
8 = Analytical and clinical chemistry

Date d'inspection : 7-8 mars 2007
Date of inspection : 7-8 mars 2007

Inspection de renouvellement (i.r)
Renewal inspection (i.r)

Date de décision du GIPC : 29 juin 2007
Date of GIPC decision: 29 juin 2007

Date de prise d'effet : 8 mars 2007
Date of implementation: 8 mars 2007

Année de première conformité : 1989
Year of the first conformity: 1989

Durée de validité: 18 mois
Time of validity: 18 months

Le Président,

Pierre CREYSSEL
Conseiller d'Etat h

CENTRE INTERNATIONAL DE TOXICOLOGIE
(CIT)
MISEREY – BP 563
27005 EVREUX CEDEX

CONFIDENTIAL

CIT
Safety & Health
Research Laboratories

SPONSOR

[redacted]

TEST ITEM

[redacted]

STUDY TITLE

EVALUATION OF SKIN SENSITIZATION POTENTIAL IN MICE USING THE LOCAL LYMPH NODE ASSAY (LLNA)

STUDY DIRECTOR

Guillaume Sire

DATE OF ISSUE

05 September 2008

TEST FACILITY

CIT
BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER

[redacted]

IFM Recherche
SAS au Capital de 846.000 €
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E-mail : CIT@citox.com
Web site . www.citox.com

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with CIT's standard operating procedures and the following principles of Good Laboratory Practice:

- OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents.
- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20.2.2004).
- Décret N° 2006-1523 du 04 décembre 2006 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 06 décembre 2006), Ministère de l'Economie, des Finances et de l'Industrie.

However, no chemical analysis of the dosage forms was performed as part of this study.
This exception is not considered to impact on the overall GLP status of the study.

The study was also conducted in compliance with the following Animal Protection regulations:

- Council Directive 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.
- Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation, OECD Environmental Health and Safety Publications, No. 19.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at CIT, BP 563, 27005 Evreux, France.

Toxicology

G. Sire Study completion date: 04 September 2008
Study Director
DESS Cellular Engineering

[redacted]

OTHER CIT SCIENTIST INVOLVED IN THE STUDY

Director of Toxicology
CIT Management

J.J. Legrand Date: 05 Sept 2008
Doctor of Veterinary Medicine

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT:

The CIT Quality Assurance Unit conducted the inspections detailed below:

Type of inspection	Dates		
	Inspection	Reported to the Study Director	Reported to Management
Study plan	12 February 2008	12 February 2008	14 February 2008
Report	19 August 2008	19 August 2008	21 August 2008

In addition, at about the same time, process-based and facility inspections relevant to this study were carried out by the Quality Assurance Unit.

The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

Marie-Christine Ottini-Bertin
CIT Quality Assurance Unit

Date: 05 Sept. 2008

[redacted]

SUMMARY

[redacted]

Lymph Node Assay (LLNA). Evaluation of local irritation was also carried out [redacted]
This study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

A preliminary test was first performed in order to define the concentrations of test item to be used in the main test.
In the main test, twenty-eight female CBA/J mice were allocated to seven groups:

- five treated groups of four animals receiving the test item [redacted] at the concentration of 0.1, 0.25, 0.5, 1 or 2.5%,
- one negative control group of four animals receiving the vehicle (propylene glycol),
- one positive control group of four animals receiving the reference item, α-hexylcinnamaldehyde (HCA), a moderate sensitizer, at the concentration of 25%.

During the induction phase, the test item, vehicle or reference item was applied over the ears (25 µL per ear) for 3 consecutive days (days 1, 2 and 3). After 2 days of resting, the proliferation of lymphocytes in the lymph node draining the application site was measured by incorporation of tritiated methyl thymidine (day 6). The obtained values were used to calculate stimulation indices (SI).

The irritant potential of the test item was assessed in parallel by measurement of ear thickness on days 1, 2, 3 and 6.

Results

The test item was not soluble in the recommended vehicles, consequently, a homogenous suspension, obtained in propylene glycol, was used for the study. The maximum practicable concentration in this vehicle was 2.5%.
Therefore, the concentrations selected for the preliminary test were 0.25, 0.5, 1 and 2.5%.

Since the test item was non-irritant in the preliminary test, the highest concentration retained for the main test was the maximal practicable concentration (2.5%).

Systemic clinical signs and mortality
No mortality and no clinical signs were observed during the study.

Local irritation
A black coloration of the skin of the ears was noted on days 2 and 3 in all animals treated at the concentrations of 1 and 2.5% and on day 6 in 2/4 animals treated at the concentration of 2.5%.
No noteworthy increase in ear thickness was observed in the animals of the treated groups.

[redacted] 8

Proliferation assay
A significant lymphoproliferation was noted in the positive control group given HCA at 25%, the study was therefore considered valid.
No noteworthy lymphoproliferation was noted at any of the tested concentrations.

The results are presented in the following table:

Treatment	Concentration (%)	Irritation level	Stimulation Index (SI)
Test item	0.1	non-irritant	1.13
Test item	0.25	non-irritant	0.72
Test item	0.5	non-irritant	0.84
Test item	1	non-irritant	0.97
Test item	2.5	non-irritant	0.76
HCA	25	-	8.59

Conclusion

Under the experimental conditions of this study, the test item [redacted] not induce delayed contact hypersensitivity in the murine Local Lymph Node Assay.

RESUME

[redacted] a induit une hypersensibilité de contact retardée par le test du "Local Lymph Node Assay" (LLNA). L'irritation locale a été également évaluée en parallèle.
L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthode

Dans un premier temps, un essai préliminaire a été réalisé afin de déterminer les concentrations de produit à utiliser dans l'essai principal.
Dans l'essai principal, 28 souris femelles CBA/J ont été réparties en 7 groupes :

- 5 groupes traités de 4 animaux recevant le produit [redacted] la concentration de 0,1 ; 0,25 ; 0,5 ; 1 ou 2,5 %,
- 1 groupe témoin négatif de 4 animaux recevant le véhicule (propylène glycol),
- 1 groupe témoin positif de 4 animaux recevant le produit de référence, α–hexylcinnamaldehyde (HCA), un sensibilisant modéré, à la concentration de 25 %.

Pendant la phase d'induction, le produit, le véhicule ou le produit de référence a été appliqué sur les oreilles (25 µL par oreille) pendant 3 jours consécutifs (jours 1, 2 et 3). Après 2 jours de repos, la prolifération lymphocytaire dans le noeud lymphatique drainant le site d'application a été mesuré par incorporation de méthyl thymidine tritiée (jour 6). Les valeurs obtenues ont été utilisées pour calculer l'indice de stimulation (IS).

Le potentiel irritant du produit a été évalué en parallèle en mesurant l'épaisseur de l'oreille aux jours 1, 2, 3 et 6.

Résultats

Le produit n'a pas été soluble dans les véhicules recommandés, par conséquent, une suspension homogène, obtenue dans le propylène glycol, a été utilisée pour l'étude. La concentration maximale utilisable dans ce véhicule a été 2,5 %.
Les concentrations retenues pour l'essai préliminaire ont été 0,25 ; 0,5 ; 1 et 2,5 %.

Le produit n'ayant pas été irritant lors de l'essai préliminaire, la concentration maximale retenue pour l'essai principal a été la concentration maximale utilisable (2,5 %).

Signes cliniques systémiques et mortalité
Aucune mortalité ni aucun signe clinique n'ont été observés pendant l'étude.

Irritation locale
Une coloration noire de la peau des oreilles a été notée aux jours 2 et 3 chez tous les animaux traités aux concentrations 1 et 2,5 % et au jour 6 chez 2/4 animaux traités à la concentration de 2,5 %. Aucune augmentation notable de l'épaisseur de l'oreille n'a été notée chez les animaux traités avec le produit.

Test de prolifération
Une lymphoprolifération significative a été notée avec le groupe témoin positif ayant reçu le HCA à 25 %, l'étude est donc considérée valide.
Aucune lymphoprolifération n'a été notée aux concentrations testées.

Les résultats sont présentés dans le tableau suivant :

Traitement	Concentration (%)	Niveau d'irritation	Indice de Stimulation (IS)
Produit	0,1	non-irritant	1,13
Produit	0,25	non-irritant	0,72
Produit	0,5	non-irritant	0,84
Produit	1	non-irritant	0,97
Produit	2,5	non-irritant	0,76
HCA	25	-	8,59

Conclusion

Dans nos conditions expérimentales, le produit [redacted] induit une hypersensibilité de contact retardée dans le test du LLNA.

1. INTRODUCTION

The aim of this study was to evaluate the potential of the test item [redacted] induce delayed contact hypersensitivity, using the murine Local Lymph Node Assay (LLNA).

This study was based on the design adopted by ICCVAM (Interagency Coordination Committee on the Validation of Alternative Methods, ICCVAM 1999) and ECETOC (Monograph No. 78 Skin sensitization Testing for the Purpose of Hazard Identification and Risk Assessment, September 2000), with the addition of the evaluation of local irritation.

The study has been designed to comply with the following guidelines:
- OECD Guideline No. 429, 24th April 2002,
- EC Directive No. 2004/73/EC, part B.42, 29th April 2004.

2. MATERIALS AND METHODS

2.1 TEST MATERIALS

2.1.1 Test item

- supplier: Arkema France
- name: [redacted]
- description: black powder
- container: one plastic flask
- date of receipt: 29 June 2007
- storage conditions: at room temperature and protected from humidity
- purity/composition: see analytical certificate
- expiry date: June 2008.

Data relating to the characterization of the test item are documented in an analytical certificate and a test item date sheet (presented in appendix 1) provided by the Sponsor.

2.1.2 Vehicle

The vehicle used was propylene glycol, batch No. S35142-236 (Aldrich, Saint-Quentin-Fallavier, France).

2.1.3 Dosage form preparation

The concentrations were expressed in % (w/v).
For the dosage form preparation at 2.5%, the test item was ground to a fine powder using a mortar and pestle, before to add the vehicle. The lower concentrations were obtained by dilution in the vehicle.
All dosage form preparations were made freshly on the morning of administration and any unused material was discarded that same day.

2.1.4 Other materials

2.1.4.1 Reference item (positive control)

The reference item (positive control) was α-hexylcinnamaldehyde (HCA), batch No. 04012JE (Aldrich, Saint-Quentin-Fallavier, France), dissolved in a mixture acetone/olive oil (4/1, v/v) at the concentration of 25% (v/v).
The preparation was made freshly on the morning of administration and any unused material was discarded that same day.

2.1.4.2 Reagent used for the proliferation assay

The reagent used for the proliferation assay was [^{3}H] methyl-thymidine (^{3}H-TdR), batch No. B505 (Amersham, Les Ulis, France).

Three days before the injections, the required quantity of ^{3}H-TdR was diluted in 0.9% NaCl (20 µCi in 250 µL of 0.9% NaCl per animal). The obtained solution was stored at +4°C and protected from light before use.

2.2 TEST SYSTEM

2.2.1 Animals

Species, strain and sex:	CBA/J mouse, nulliparous and non-pregnant females.
Reason for this choice:	species generally accepted by regulatory authorities for this type of study. Females have been chosen since this sex is recommended by regulatory authorities for this type of study.
Age/weight:	on the first day of the treatment period, the animals of the preliminary test were approximately 10 weeks old and the animals of the main test were approximately 9 weeks old and had a mean body weight ± standard deviation of 21.2 ± 1.1 g.
Number:	4 females for the preliminary test, 28 females for the main test.
Breeder:	Janvier, Le Genest-Saint-Isle, France.
Acclimation:	at least 5 days before the beginning of the study.
Allocation to groups:	animals were assigned to the treatment groups by hand procedure.
Identification:	individually by a number on the tail.

2.2.2 Environmental conditions

The conditions in the animal room were set as follows:
- temperature: 22 ± 2°C
- relative humidity: 30 to 70%
- light/dark cycle: 12 h/12 h (7:00-19:00)
- ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity are under continuous control and recording. The records are checked daily and filed. In addition to these daily checks, the housing conditions and corresponding instrumentation and equipment are verified and calibrated at regular intervals.
The animals were housed individually in disposable crystal polystyrene cages (22.00 cm x 8.50 cm x 8.00 cm). Each cage contained autoclaved sawdust (SICSA, Alfortville, France). Sawdust is analyzed by the supplier for composition and contaminant levels.

2.2.3 Food and water

All animals had free access to SSNIFF R/M-H pelleted maintenance diet (SSNIFF Spezialdiäten GmbH, Soest, Germany) and tap water (filtered using a 0.22 micron filter) contained in bottles.
Each batch of diet is analyzed for composition and contaminant level by the supplier.
The diet formula is presented in appendix 2.

Bacteriological and chemical analyses of water, including the detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed regularly by external laboratories. The results of these analyses are archived at CIT.

No contaminants are known to be present in the diet, drinking water or sawdust at levels which may be expected to interfere with or prejudice the outcome of the study.

2.3 TREATMENT

2.3.1 Preliminary test

To assess the irritant potential of the test item (through ear thickness measurement), a preliminary test was performed on a small number of animals, as follows:

- the test item was prepared at the concentrations of 2.5, 1, 0.5 and 0.25%,
- for 3 consecutive days, the animals received applications of 25 µL of the dosage form preparations to the external surface of both ears (one concentration per ear),
- measurement of the ear thickness (using a micrometer) was performed each day before treatment and 72 hours after the last application.

2.3.2 Main test

2.3.2.1 Study design

The concentrations of test item were selected according to the criteria specified in the International Guideline and on the basis of the results of the solubility and preliminary assays.

The study design was as follows:

Groups	Number of animals	Treatment	Concentration (%)
1	4 females	Vehicle	0
2	4 females	Test item	0.1
3	4 females	Test item	0.25
4	4 females	Test item	0.5
5	4 females	Test item	1
6	4 females	Test item	2.5
7	4 females	HCA	25

2.3.2.2 Administration of the test materials

On days 1, 2 and 3, a dose-volume of 25 µL of the control or dosage form preparations was applied to the dorsal surface of both ears, using an adjustable pipette fitted with a plastic tip.
In order to avoid licking and to ensure an optimized application of the test materials, the animals were placed under light isoflurane anesthezia during the administration.
No massage was performed but the tip was used to spread the preparation over the application sites. No rinsing was performed between each application.

2.4 CLINICAL EXAMINATIONS

2.4.1 Clinical signs, morbidity and mortality

The animals were observed at least once a day during the study for clinical signs, signs of morbidity or mortality.

2.4.2 Body weight

The animals were weighed individually on the first day of the study (day 1) and on the day of sacrifice (day 6).

2.4.3 Ear thickness measurements and recording of local reactions

Ear thickness measurements and recording of local reactions were performed in order to assess any possible irritant effect of the test item, as possible irritancy may be involved in false positive lymphoproliferative responses.

On days 1, 2 and 3 (before each cutaneous application) and on day 6 (after sacrifice), the thickness of the left ear of each animal of the vehicle control and treated groups was measured using a micrometer.
No measurement of ear thickness was performed for the animals of the positive control group.
Any irritation reaction (erythema and edema) was recorded in parallel. Any other observation (coloration, presence of residual test item, ...) was noted.

The irritation level of the test item was determined according to the following table:

% increase in ear thickness between day 1 and day 3 or 6	Irritation level	Interpretation
< 10%	I	Non-irritant
10 - 30%	II	Slightly irritant
> 30%	III	Irritant

2.5 PROLIFERATION ASSAY

2.5.1 Intravenous injection of ^{3}H-TdR and sampling of auricular lymph nodes

Lymph node cell proliferative responses were measured as described by Kimber and Dearman (1991). On day 6, all animals of all groups received a single intravenous injection of 250 µL of 0.9% NaCl containing 20 µCi of ^{3}H-TdR (specific activity of 25 Ci/mmol) via the tail vein. Approximately 5 hours later, the animals were killed by cervical dislocation and the auricular lymph nodes were excised. The lymph nodes were pooled for each experimental group.

2.5.2 Preparation of auricular lymph node cell suspensions and determination of proliferation

For each experimental group, a single cell suspension of auricular lymph node cells (ALNC) was prepared by mechanical dissagregation in Petri dishes with the plunger of a syringe. Cell suspensions were washed with 15 mL of 0.9% NaCl and pellets obtained were re-suspended in 0.9% NaCl for numeration of lymphocytes (cellularity) and determination of their viability by exclusion of trypan blue. Each cell suspension was then centrifuged and pellets were precipitated with 3 mL of 5% (w/v) trichloroacetic acid (TCA) in purified water at +4°C overnight. After a last centrifugation, the pellets were precipitated with 1 mL of 5% TCA. Three mL of Ultima Gold^{XR} scintillation fluid (Packard) were added in order to measure incorporation of ^{3}H-TdR using β-scintillation counting.
The results were expressed as disintegration's/mn (dpm) per group and per node.
Stimulation Indices (SI) were calculated according to the following formula:

$$SI = \frac{\text{dpm of treated group}}{\text{dpm of control group}}$$

2.5.3 Interpretation of results

The test item was considered as a skin sensitizer when the SI for a dose group is ≥ 3. Other relevant criteria such as cellularity, radioactivity levels and ear thickness were also taken into account for the interpretation of results.

2.6 ARCHIVING

The following study materials are archived by CIT, 27005 Evreux, France, for 10 years after the end of the *in vivo* phase of the study:

- Study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments.

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost). The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.
In addition, raw data not specific to the study including, but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration, are also archived by CIT for at least 30 years.

2.7 CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date
Experimental starting date (solubility assay)	13 March 2008
First day of treatment of the preliminary test	18 March 2008
First day of treatment of the main test	26 March 2008
Day of injection of ^{3}H-TdR and ALNC collection	31 March 2008
Experimental completion date	04 September 2008

2.8 STUDY PLAN ADHERENCE

The study was performed in accordance with the [redacted]d subsequent amendments. There were no deviations from the agreed Study plan.

3. RESULTS

3.1 CHOICE OF THE VEHICLE

The test item was not soluble in the recommended vehicles, consequently, a homogenous suspension, obtained in propylene glycol, was used for the study. The maximum practicable concentration in this vehicle was 2.5%.

3.2 PRELIMINARY TEST

The results of the preliminary test are presented in table 1.

A black coloration of the skin of the ears was observed at the concentrations of 1 and 2.5% on days 2 and 3.
The test item was non-irritant in the preliminary test, whatever the concentrations tested.
The highest concentration retained for the main test was therefore the maximal practicable concentration (2.5%).

3.3 MAIN TEST

3.3.1 Systemic clinical signs and mortality

No clinical signs and no mortality were observed during the study.

3.3.2 Body weight (table 2)

The body weight change of treated animals was similar to that of control animals.

3.3.3 Local irritation (tables 3 and 4)

A black coloration of the skin of the ears was noted on days 2 and 3 in all animals treated at the concentrations of 1 and 2.5% and on day 6 in 2/4 animals treated at the concentration of 2.5%.
No noteworthy increase in ear thickness was observed in the animals of the treated groups.

3.3.4 Proliferation assay

Results of proliferation assay are presented in table 5.

The quantity of cells obtained in each group was satisfactory and the cellularity correlated with incorporation of ^{3}H-TdR. The cell viability was higher than 70% in each group.

In the positive control group given HCA at the concentration of 25%, a moderate increase in cellularity and a stimulation index exceeding the threshold value of 3 (SI = 8.59) were noted. The study was therefore considered valid.

No noteworthy lymphoproliferation was noted with the test item at any of the tested concentrations.

4. CONCLUSION

Under the experimental conditions of this study, the test item [redacted] did not induce delayed contact hypersensitivity in the murine Local Lymph Node Assay.

Table 1: Results of the preliminary test (ear thickness measurements)

Number Animal	Concentration %		D1		D2		D3		D6		%
			Ear Thickness	Local reaction	Ear Thickness	Local reaction	Ear Thickness	Local reaction	Ear Thickness	Local reaction	
Female 301	2.5	RE	0.24	0	0.25	0/C	0.26	0/C	0.26	0	8.33
Female 301	1	LE	0.25	0	0.25	0/C	0.25	0/C	0.27	0	8.00
Female 302	2.5	RE	0.24	0	0.24	0/C	0.24	0/C	0.24	0	0.00
Female 302	1	LE	0.24	0	0.24	0/C	0.24	0/C	0.23	0	-4.17
Female 303	0.5	RE	0.24	0	0.24	0	0.24	0	0.25	0	4.17
Female 303	0.25	LE	0.25	0	0.25	0	0.25	0	0.25	0	0.00
Female 304	0.5	RE	0.25	0	0.25	0	0.25	0	0.25	0	0.00
Female 304	0.25	LE	0.25	0	0.24	0	0.25	0	0.26	0	4.00

RE = right ear
LE = left ear
D = day
0 = no cutaneous reaction
C = black coloration of the ears
% = percentage of ear thickness increase compared to day 1

Table 2: Individual body weight and body weight gain (g)

Groups	Animal No.	Days 1	6	(1)
1	01	18.9	19.4	0.5
	02	21.3	20.9	-0.4
	03	21.0	21.4	0.4
	04	18.8	19.7	0.9
	M	20.0	20.4	0.3
	SD	1.3	1.0	0.5
2	05	21.1	21.9	0.8
	06	20.4	21.2	0.8
	07	22.0	21.9	-0.1
	08	21.6	22.0	0.4
	M	21.3	21.8	0.5
	SD	0.7	0.4	0.4
3	09	22.6	22.0	-0.6
	10	19.4	20.2	0.8
	11	21.8	21.5	-0.3
	12	20.2	21.3	1.1
	M	21.0	21.3	0.3
	SD	1.5	0.8	0.8
4	13	21.4	19.1	-2.3
	14	20.6	21.0	0.4
	15	19.7	19.5	-0.2
	16	21.3	22.3	1.0
	M	20.8	20.5	-0.3
	SD	0.8	1.5	1.4

(1) = body weight gain
M = mean
SD = standard deviation

Table 2 (continued)

Groups	Animal No.	Days 1	Days 6	(1)
5	17	20.6	21.0	0.4
	18	20.5	21.5	1.0
	19	22.1	22.2	0.1
	20	21.5	21.4	-0.1
	M	21.2	21.5	0.3
	SD	0.8	0.5	0.5
6	21	21.7	22.6	0.9
	22	22.0	22.3	0.3
	23	23.8	22.5	-1.3
	24	22.6	21.2	-1.4
	M	22.5	22.2	-0.4
	SD	0.9	0.6	1.2
7	25	21.6	22.5	0.9
	26	22.0	22.9	0.9
	27	22.1	19.5	-2.6
	28	21.1	21.7	0.6
	M	21.7	21.7	-0.1
	SD	0.5	1.5	1.7

(1) = body weight gain
M = mean
SD = standard deviation

[redacted] 21

Table 3: Evaluation of cutaneous reactions

Groups	Dosage form	Animal No.	Days			
			1	2	3	6
1	vehicle	01	0	0	0	0
		02	0	0	0	0
		03	0	0	0	0
		04	0	0	0	0
2	test item	05	0	0	0	0
	0.1%	06	0	0	0	0
		07	0	0	0	0
		08	0	0	0	0
3	test item	09	0	0	0	0
	0.25%	10	0	0	0	0
		11	0	0	0	0
		12	0	0	0	0
4	test item	13	0	0	0	0
	0.5%	14	0	0	0	0
		15	0	0	0	0
		16	0	0	0	0
5	test item	17	0	0/C	0/C	0
	1%	18	0	0/C	0/C	0
		19	0	0/C	0/C	0
		20	0	0/C	0/C	0
6	test item	21	0	0/C	0/C	0
	2.5%	22	0	0/C	0/C	0/C
		23	0	0/C	0/C	0/C
		24	0	0/C	0/C	0

0 = no cutaneous reaction
C = black coloration of the ears
vehicle = propylene glycol

[redacted]

Table 4: Ear thickness measurements (mm)

Groups	Dosage form	Animal No.	Days 1	2	d1	3	d2	6	d3
1	vehicle	01	0.26	0.25	-0.01	0.25	-0.01	0.25	-0.01
		02	0.26	0.26	0.00	0.26	0.00	0.25	-0.01
		03	0.26	0.27	0.01	0.26	0.00	0.25	-0.01
		04	0.25	0.25	0.00	0.24	-0.01	0.25	0.00
		M	0.26	0.26	0.00	0.25	-0.01	0.25	-0.01
		SD	0.01	0.01	0.01	0.01	0.01	0.00	0.01
		% (*)			0.00		-1.94		-2.91
2	test item	05	0.25	0.25	0.00	0.24	-0.01	0.24	-0.01
	0.1%	06	0.26	0.26	0.00	0.25	-0.01	0.25	-0.01
		07	0.26	0.25	-0.01	0.25	-0.01	0.25	-0.01
		08	0.25	0.24	-0.01	0.26	0.01	0.27	0.02
		M	0.26	0.25	-0.01	0.25	-0.01	0.25	0.00
		SD	0.01	0.01	0.01	0.01	0.01	0.01	0.02
		% (*)			-1.96		-1.96		-0.98
3	test item	09	0.27	0.26	-0.01	0.26	-0.01	0.26	-0.01
	0.25%	10	0.25	0.24	-0.01	0.24	-0.01	0.24	-0.01
		11	0.26	0.25	-0.01	0.25	-0.01	0.25	-0.01
		12	0.26	0.25	-0.01	0.26	0.00	0.25	-0.01
		M	0.26	0.25	-0.01	0.25	-0.01	0.25	-0.01
		SD	0.01	0.01	0.00	0.01	0.01	0.01	0.00
		% (*)			-3.85		-2.88		-3.85

M = mean
SD = standard deviation
(*) = percentage of ear thickness increase compared to day 1
d1 = difference of ear thickness between day 2 and day 1
d2 = difference of ear thickness between day 3 and day 1
d3 = difference of ear thickness between day 6 and day 1
vehicle = propylene glycol

[redacted] 23

Table 4 (continued)

Groups	Dosage form	Animal No.	Days 1	2	d1	3	d2	6	d3
4	test item 0.5%	13	0.25	0.24	-0.01	0.25	0.00	0.25	0.00
		14	0.25	0.25	0.00	0.25	0.00	0.25	0.00
		15	0.25	0.26	0.01	0.25	0.00	0.26	0.01
		16	0.25	0.25	0.00	0.25	0.00	0.25	0.00
		M	0.25	0.25	0.00	0.25	0.00	0.25	0.00
		SD	0.00	0.01	0.01	0.00	0.00	0.01	0.01
		% (*)			0.00		0.00		1.00
5	test item 1%	17	0.25	0.26	0.01	0.25	0.00	0.26	0.01
		18	0.26	0.25	-0.01	0.26	0.00	0.25	-0.01
		19	0.27	0.25	-0.02	0.26	-0.01	0.26	-0.01
		20	0.25	0.25	0.00	0.25	0.00	0.24	-0.01
		M	0.26	0.25	-0.01	0.26	0.00	0.25	-0.01
		SD	0.01	0.01	0.01	0.01	0.01	0.01	0.01
		% (*)			-1.94		-0.97		-1.94
6	test item 2.5%	21	0.25	0.25	0.00	0.26	0.01	0.26	0.01
		22	0.25	0.25	0.00	0.25	0.00	0.25	0.00
		23	0.25	0.25	0.00	0.24	-0.01	0.24	-0.01
		24	0.25	0.25	0.00	0.26	0.01	0.26	0.01
		M	0.25	0.25	0.00	0.25	0.00	0.25	0.00
		SD	0.00	0.00	0.00	0.01	0.01	0.01	0.01
		% (*)			0.00		1.00		1.00

M = mean
SD = standard deviation
(*) = percentage of ear thickness increase compared to day 1
d1 = difference of ear thickness between day 2 and day 1
d2 = difference of ear thickness between day 3 and day 1
d3 = difference of ear thickness between day 6 and day 1

[redacted]

[redacted] 24

Table 5: Study results

Groups	Treatment and concentrations	Cell count viable	Cell count dead	Viability (%)	Amount of cells ($x 10^6$ cells)	Cellularity index	Number of nodes per group	dpm per group	dpm per node	Stimulation index (SI)	Increase in ear thickness (% between day 1 and day 6)	Irritation level	EC_3 value
1	Vehicle	103	8	92.79	5.15	[redacted]	8	576.81	72.10	[redacted]	-2.91	[redacted]	[redacted]
2	Test item 0.1%	183	1	99.46	9.15	1.78	8	654.34	81.79	1.13	-0.98	I	NA
3	Test item 0.25%	81	3	96.43	4.05	0.79	8	416.37	52.05	0.72	-3.85	I	
4	Test item 0.5%	82	7	92.13	4.10	0 80	8	484.86	60.61	0.84	1.00	I	
5	Test item 1%	69	18	79 31	3.45	0.67	8	558.54	69 82	0 97	-1.94	I	
6	Test item 2.5%	88	6	93.62	4.40	0.85	8	436.90	54.61	0.76	1.00	I	
7	HCA 25%	214	18	92.24	21.40	4.16	8	4956.76	619.60	8.59	[redacted]	[redacted]	[redacted]

$$\text{viability} = \frac{\text{viable cells}}{\text{viable cells + dead cells}} \times 100$$

$$\text{cellularity index} = \frac{\text{amount of cells } (x 10^6 \text{ cells}) \text{ in the treated group}}{\text{amount of cells } (x 10^6 \text{ cells}) \text{ in the vehicle group}}$$

$$\text{stimulation index} = \frac{\text{dpm of treated group}}{\text{dpm of control group}}$$

[redacted]

dpm = disintegrations per minute
HCA = α-hexylcinnamaldehyde
1 = non-irritant (increase in ear thickness < 10%)
EC_3 value = theoretical concentration resulting in a SI value of 3

[redacted] 25

APPENDICES

[redacted] 26

1. Test article description and analytical certificate

[redacted]

27

[redacted]

IDENTITY

Test article name	[redacted]
Chemical name	
CAS number	
EINECS number	
Origin	
Batch number	
Arkema filing number	

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	black powder
Particule size	:	30 µm (approximately)
Specific Gravity	:	2,1 kg/m3 at 20°C
Autoignition temperature	:	> 400 °C (standard : NF EN 50281-2-1)
Solubility	:	in water : insoluble

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See Safety Data Sheet.

STORAGE AND DISPOSAL

Storage	:	Keep hermetically closed in a dry, cool and well-ventiled place .
Expiry date	:	June 2008
Disposal	:	Incineration

[redacted]

28

[redacted]

Date 5 juin 2007

[redacted]

DETERMINATION / *ITEM*	RESULTAT / *RESULT*	Référence de la méthode d'analyse / *Analysis reference*
Powder characteristics		
Ash content (%)	7.6%	ATG
[redacted]	70	[redacted]
[redacted]	[redacted]	[redacted]

Nom du responsable du laboratoire/ *Laboratory Director* :

Signature

[redacted]

2. Diet formula

SSNIFF R/M-H

Complete diet for rats/mice - maintenance

Crude proteins	19.00 %
Crude fat	3.30 %
Crude fiber	4.90 %
Crude ash	6.70 %

Constituents

Calcium	1.00 %
Phosphorus	0.70 %
Sodium	0.25 %
Magnesium	0.20 %
Potassium	0.90 %

Amino Acids

Lysine	1.00 %
Methionine	0.30 %
Cystine	0.30 %
Glycine	0.90 %
Leucine	1.30 %
Isoleucine	0.70 %
Arginine	1.20 %
Phenylalanine	0.90 %
Tryptophan	0.25 %
Histidine	0.50 %
Tyrosine	0.60 %
Aspartic acid	1.70 %
Glutaminic acid	3.80 %
Valine	0.90 %
Threonine	0.70 %

Vitamins (je kg)

A	15,000 IE
D3	1,000 IE
E	100 mg
B1	10 mg
B2	20 mg
B6	12 mg
B12	80 µg
Biotin	400 µg
Pantothenic acid	30 mg
Choline	1,600 mg
Folic acid	4 mg
Nicotic acid	60 mg
K3	5 mg
Inositol	50 mg

Trace elements (je kg)

Manganese	90 mg
Copper	12 mg
Zinc	75 mg
Iodine	2 mg
Iron	220 mg
Selenium	0.2 mg
Cobalt	2 mg

ME (je kg) **12.2 MJ**

Item numbers

V1530 Meal
V1531 Micromeal
V1534 Pellets 10 mm
V1535 Pellets 15 mm

[redacted] 31

3. Historical data

[redacted]

Historical data
Skin sensitization potential in mice (CBA/J strain)
using the Local Lymph Node Assay (LLNA)
Vehicle control Propylene Glycol
from December 2004 to December 2006

	Amount of cells (x10^6 cells)	dpm/node	increase in ear thickness (%)
minimum	**2.75**	**33.28**	**-4.63**
maximum	**7.90**	**76.64**	**1.02**
Mean	5.03	47.93	-0.98
SD	1.65	10.60	1.78
Nb	17		

SD = Standard deviation
Nb = number of values

4. CIT GLP certificate

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

Paris, le - 9 JUIL. 2007

Objet : Evaluation de la conformité aux Bonnes Pratiques de Laboratoires (BPL) selon les directives 2004/9/CE et 2004/10/CE du 11 février 2004.

Subject : Assessment of compliance with Good Laboratory Practices (GLP) under the EC directives 2004/9 and 2004/10 of 11 February 2004.

Consécutivement à votre engagement vis-à-vis du GIPC et du COFRAC et en application du décret n° 2006-1523 du 4 décembre 2006 concernant les bonnes pratiques de laboratoires et modifiant le décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Laboratoires a décidé pour votre installation du statut suivant :
Following your engagement vis-à-vis the GIPC and COFRAC and in application of the decree n° 2006-1523 of 4 December 2006 relating to the good laboratory practices and modifying the decree n° 81-278 of 25 March 1981 giving birth to an interministerial group of chemical products (GIPC), I confirm to you that the GIPC, given the results of the inspection realised by the French Committee of accreditation (COFRAC) – Laboratory Section has taken the following decision relating to your installation:

Respect des principes de BPL
Respect of the GLP principles

Domaines de reconnaissance:
1 - essais physico-chimiques
2 - études de toxicité
3 - études de mutagénicité
4 - études écotoxicologiques sur les organismes aquatiques et terrestres
8 - méthodes de chimie analytique et clinique

Areas of expertise :
1 = Physico-chemical testing
2 = Toxicity studies
3 = Mutagenicity studies
4 = Environmental toxicity studies on aquatic or terrestrial organisms
8 = Analytical and clinical chemistry

Date d'inspection : 7-8 mars 2007
Date of inspection : 7-8 mars 2007

Inspection de renouvellement (i.r)
Renewal inspection (i.r)

Date de décision du GIPC : 29 juin 2007
Date of GIPC decision: 29 juin 2007

Date de prise d'effet : 8 mars 2007
Date of implementation: 8 mars 2007

Année de première conformité : 1989
Year of the first conformity: 1989

Durée de validité: 18 mois
Time of validity: 18 months

Le Président,

Pierre CREYSSEL
Conseiller d'Etat h

CENTRE INTERNATIONAL DE TOXICOLOGIE
(CIT)
MISEREY – BP 563
27005 EVREUX CEDEX

CONFIDENTIAL

CIT
Safety & Health
Research Laboratories

SPONSOR

[redacted]

TEST ITEM

[redacted]

STUDY TITLE

ACUTE DERMAL IRRITATION
IN RABBITS

STUDY DIRECTOR

Catherine Pelcot

DATE OF ISSUE

25 April 2008

TEST FACILITY

CIT
BP 563 - 27005 Evreux - France

LABORATORY STUDY NUMBER

[redacted]

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

The study was performed in compliance with the principles of Good Laboratory Practice as described in:

- OECD Principles of Good Laboratory Practice (as revised in 1997), ENV/MC/CHEM (98) 17 and all subsequent OECD consensus documents.
- Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonization of laws, regulations and administrative provisions relating to the application of the Principles of Good Laboratory Practice and the verification of their applications for tests on chemical substances (OJ No. L50 of 20.2.2004).
- Décret N° 2006-1523 du 04 décembre 2006 concernant les Bonnes Pratiques de Laboratoire (Journal Officiel du 06 décembre 2006), Ministère de l'Economie, des Finances et de l'Industrie.

The study was also conducted in compliance with the following Animal Protection regulations:

- Council Directive 86/609/EEC of 24th November 1986 on the harmonization of laws, regulations or administrative provisions relating to the protection of animals used for experimental or other scientific purposes.
- Guidance document on the recognition, assessment, and use of clinical signs as humane endpoints for experimental animals used in safety evaluation, OECD Environmental Health and Safety Publications, No. 19.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained during the performance of the study.

This study was performed at CIT, BP 563, 27005 Evreux, France.

Toxicology

C. Pelcot
Study Director

Study completion date: 22 April 2008

OTHER CIT SCIENTIST INVOLVED IN THE STUDY

Director of Toxicology
CIT Management

J.J. Legrand Date: 26 April 2007
Doctor of Veterinary Medicine

STATEMENT OF QUALITY ASSURANCE UNIT

Inspections performed at CIT:

The CIT Quality Assurance Unit conducted the inspections detailed below:

Type of inspection	Dates		
	Inspection	Reported to the Study Director	Reported to Management
Study plan	27 July 2007	27 July 2007	02 August 2007
Report	21 March 2008	27 March 2008	08 April 2008

In addition, at about the same time, process-based and facility inspections relevant to this study were carried out by the Quality Assurance Unit.

The inspections were performed in compliance with CIT Quality Assurance Unit procedures and the principles of Good Laboratory Practices.

The final report is considered to constitute an accurate and complete reflection of the study raw data.

A DE CECCO Date: 25 Apr 2008
CIT Quality Assurance Unit

SUMMARY

[redacted] in rabbits according to OECD (No. 404, 24th April 2002) and EC (2004/73/EC, B.4, 29th April 2004) guidelines.
The study was conducted in compliance with the principles of Good Laboratory Practice Regulations.

Methods

The test item was first applied for periods of 3 minutes, 1 hour and 4 hours to a single male New Zealand White rabbit. Since the test item was neither severely irritant nor corrosive on this first animal, it was then applied simultaneously for 4 hours to two other animals.

A single dose of 500 mg of the test item in its original form was applied to the closely-clipped skin of one flank. The test item was held in contact with the skin by means of a semi-occlusive dressing.

Cutaneous reactions were observed approximately 1 hour, 24, 48 and 72 hours after removal of the dressing and then daily until reversibility of cutaneous reactions (day 8).
The mean values of the scores for edema were calculated for each animal.

Results

After a 3-minute exposure (one animal)
No cutaneous reactions were observed.
A grey coloration of the skin was noted from day 1 until day 4.

After a 1-hour exposure (one animal)
A grey coloration of the skin was noted from day 1 until day 4. This coloration could have masked a possible very slight erythema on day 1. No cutaneous reactions were observed from day 2 until day 4.

After a 4-hour exposure (three animals)
A grey coloration of the skin was noted in all the animals all over the observation period. This coloration could have masked a possible very slight or well-defined erythema from day 1 until day 2, 3 or 4.
A very slight erythema was noted in 1/3 animals on days 4 and 5. A dryness of the skin was noted in 2/3 animals between day 4 and day 7.

Due to the coloration of the skin, the mean scores over 24, 48 and 72 hours for each animal were not calculable for erythema. For edema, the mean scores over 24, 48 and 72 hours for each animal were 0.0, 0.0 and 0.0. However, taking into account the possible erythema masked by the coloration, the maximal mean values over 24, 48 and 72 hours for erythema could be: 0.3, 1.0 and 1.3.

Conclusion

Under the experimental conditions of this study, when applied topically to rabbits, the test item [redacted] conclusions about its skin irritation potential.

However, taking into account the possible maximal mean values for erythema, the test item [redacted] according to the classification criteria laid down in Council Directive 67/548/EEC (and subsequent adaptations), the test item should not be classified as irritating to the skin.

RESUME

[redacted]
chez le Lapin selon les lignes directrices de l'OCDE (n° 404, 24 avril 2002) et de la CEE (2004/73/CEE, B.4, 29 avril 2004).
L'étude a été réalisée conformément aux règles de Bonnes Pratiques de Laboratoire.

Méthode

Le produit a d'abord été appliqué pendant 3 minutes, 1 heure et 4 heures sur 1 seul Lapin mâle New Zealand White. Le produit n'ayant pas montré de propriétés sévèrement irritantes ou corrosives sur ce premier animal, il a ensuite été appliqué simultanément pendant 4 heures sur 2 autres Lapins.

Une dose unique de 500 mg de produit tel quel a été appliquée sur une surface de peau tondue au niveau d'un des flancs. Le produit a été maintenu en contact avec la peau au moyen d'un pansement semi-occlusif.

Les réactions cutanées ont été observées environ 1, 24, 48 et 72 heures après l'enlèvement du pansement puis quotidiennement jusqu'à réversibilité complète des réactions cutanées (jour 8).
La moyenne des scores pour l'oedème a été calculée pour chaque animal.

Résultats

Après une exposition de 3 minutes (1 animal)
Aucune réaction cutanée n'est observée.
Une coloration grise de la peau est notée du jour 1 au jour 4.

Après une exposition de 1 heure (1 animal)
Une coloration grise de la peau est notée du jour 1 au jour 4. Cette coloration a pu masquer un éventuel érythème très léger au jour 1. Aucune réaction cutanée n'est observée du jour 2 au jour 4.

Après une exposition de 4 heures (3 animaux)
Une coloration grise de la peau est notée chez tous les animaux sur toute la période d'observation. Cette coloration a pu masquer un éventuel érythème très léger ou bien défini du jour 1 au jour 2, 3 ou 4.
Un érythème très léger est noté chez 1/3 animal aux jours 4 et 5. Une sécheresse cutanée est notée chez 2/3 animaux entre le jour 4 et le jour 7.

En raison d'une lecture masquée de l'érythème liée à la coloration de la peau par le produit, les scores moyens pour chaque animal après 24, 48 et 72 heures ne sont pas calculables pour l'érythème. Pour l'oedème, les scores moyens calculés sont de 0,0, 0,0 et 0,0. Cependant, en tenant compte de l'éventuel érythème masqué par la coloration, les scores moyens maximum après 24, 48 and 72 heures pour l'érythème pourraient être : 0,3, 1,0 et 1,3.

[redacted]

Conclusion

Dans les conditions expérimentales de cette étude par voie cutanée chez le Lapin, le produit [redacted] empêchant de conclure sur son potentiel irritant.

Cependant, en tenant compte des éventuels scores moyens maximum pour l'érythème, le produit [redacted] les critères de classification décrits dans la Directive 67/548/CEE (et ses adaptations), le produit ne devrait pas être classé comme irritant pour la peau.

1. INTRODUCTION

The objective of this study was to evaluate the potential of the test item [redacted] to induce skin irritation following a single topical application to rabbits.

In the assessment of the toxic characteristics of a test item, determination of the irritant and/or corrosive effects on the skin of mammals is an important initial step. Information derived from this test serves to indicate the possible hazards likely to arise from exposure of the skin to the test item.

This study was conducted in compliance with:
- OECD guideline No. 404, 24th April 2002,
- EC Directive No. 2004/73/EC, B.4, 29th April 2004.

2. MATERIALS AND METHODS

2.1 TEST ITEM

2.1.1 Identification

[redacted]

- Description at receipt: black powder
- container: one plastic flask
- date of receipt: 29 June 2007
- storage conditions: at room temperature and protected from humidity
- composition: see analytical certificate
- expiry date: June 2008.

Data relating to the characterization of the test item are documented in a test article description and in an analytical certificate (presented in appendix 1) provided by the Sponsor.

2.1.2 Dosage form preparation

The test item was used in its original form.
Fresh dosage form preparations were made by the CIT Pharmacy on the morning of administration and any unused material was discarded that same day.

The pH of the test item at the concentration of 1% in purified water was not measurable (non soluble and colored test item).

2.2 TEST SYSTEM

2.2.1 Animals

Sex, species, strain: male New Zealand White rabbits.
Reason for this choice: species generally accepted by regulatory authorities for this type of study.
Breeder: Grimaud frères selection S.A.S., La Corbière, Roussay, France.
Number: three animals were used, as recommended by the international guidelines.
Age/weight: on the day of treatment, the animals were 2 to 4 months old and had a mean body weight ± standard deviation of 2.5 ± 0.1 kg.
Acclimation: at least 5 days before the beginning of the study.
Identification: individual metal ear tag.

2.2.2 Environmental conditions

The conditions in the animal room were set as follows:
. temperature: 18 ± 3°C
. relative humidity: 30 to 70%
. light/dark cycle: 12 h/12 h
. ventilation: approximately 12 cycles/hour of filtered, non-recycled air.

The temperature and relative humidity were under continuous control and recording. The records were checked daily and filed. In addition to these daily checks, the housing conditions and corresponding instrumentation and equipment were verified and calibrated at regular intervals.
The animals were housed individually in Techniplast (64 cm x 63 cm x 30 cm) or Pajon (50 cm x 57 cm x 75 cm) cages.
Each cage was equipped with a food container and a water bottle.

2.2.3 Food and water

During the study, the animals had free access to 110C pelleted diet (SAFE, Villemoisson, Epinay-sur-Orge, France).
Food is analyzed regularly by the supplier for composition and contaminant levels.
The diet formula is presented in appendix 2.

Drinking water filtered by a FG Millipore membrane (0.22 micron) was provided *ad libitum*.
Bacteriological and chemical analyses of water are performed regularly by external laboratories. These analyses include the detection of possible contaminants (pesticides, heavy metals and nitrosamines).

No contaminants were known to have been present in the diet or drinking water at levels which may be expected to have interfered with or prejudiced the outcome of the study.

2.3 TREATMENT

2.3.1 Preparation and selection of the animals

The day before treatment, both flanks of each animal were clipped using electric clippers and just before treatment, the skin of each animal was examined in order to check the absence of any signs of skin irritation.

2.3.2 Application of the test item

The test item was first evaluated on a single animal (No. 513/474). The durations of exposure were 3 minutes, 1 hour and 4 hours.
Since the test item was neither severely irritant nor corrosive on this first animal, it was then applied simultaneously for 4 hours to two other animals (Nos. 483 and 484).

Doses of 500 mg of the test item in its original form were placed on a gauze pad moistened with purified water, which was then applied to an area of approximately 6 cm^2 of the anterior left flank (application for 3 minutes), the anterior right flank (application for 1 hour) or the posterior right flank (application for 4 hours) of the animals.

The gauze pad was held in contact with the skin by means of an adhesive hypoallergenic aerated semi-occlusive dressing and a restraining bandage.

The untreated skin served as control.

After removal of the dressing, any residual test item was wiped off by means of a dry cotton pad or a cotton pad moistened with acetone then with water.

2.4 CUTANEOUS EXAMINATIONS

2.4.1 Duration of the observation period

The skin was examined approximately 1 hour, 24, 48 and 72 hours after removal of the dressing. Since there were persistent irritation reactions at 72 hours, the observation period was extended up to their complete reversibility (day 8).

2.4.2 Description and evaluation of cutaneous reactions

Dermal irritation was evaluated for each animal according to the following scoring scale:

Erythema and eschar formation:

. no erythema	0
. very slight erythema (barely perceptible)	1
. well-defined erythema	2
. moderate to severe erythema	3
. severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema formation

. no edema	0
. very slight edema (barely perceptible)	1
. slight edema (edges of area well-defined by definite raising)	2
. moderate edema (raised approximately 1 millimeter)	3
. severe edema (raised more than 1 millimeter and extending beyond area of exposure)	4

Any other lesions were noted.

2.5 BODY WEIGHT

Each animal was weighted at the beginning (day of treatment) and at the end of the observation period.

2.6 INTERPRETATION OF RESULTS

The results obtained were evaluated in conjunction with the nature and the reversibility of the findings observed.

2.6.1 Interpretation of results

2.6.1.1 Criteria for irritation

A substance or a preparation is considered to be irritating to the skin if, when it is applied to healthy intact animal skin for up to 4 hours, significant inflammation is caused and which persists for 24 hours or more after the end of the exposure period.

2.6.1.2 Criteria for corrosion

A substance or a preparation is considered to be corrosive if, when it is applied to healthy intact animal skin, it produces full thickness destruction of skin tissue on at least one animal during the test for skin irritation, or if the result can be predicted (for example: from strongly acid or alkaline reactions).

All scores obtained at each reading time (24, 48 and 72 hours) for an effect are used for calculating the respective mean values.

2.7 ARCHIVING

The following study materials are archived by CIT, 27005 Evreux, France, for 10 years after the end of the *in vivo* phase of the study:

- Study plan and possible amendments,
- raw data,
- correspondence,
- final report and possible amendments.

On completion of this period, the archived study materials will be returned to the Sponsor, or may be archived at CIT for a further period (at additional cost). The total duration of archiving (depending on regulations) will be the responsibility of the Sponsor.
In addition, raw data not specific to the study including, but not limited to, certificates of analyses for food, water and bedding (if applicable) and records of environmental data and equipment calibration, are also archived by CIT for at least 30 years.

2.8 CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date
Experimental starting date (day of treatment of the first animal)	07 August 2007
Experimental completion date (end of the observation period)	16 August 2007

2.9 STUDY PLAN ADHERENCE

The study was performed in accordance w[redacted] and subsequent amendments, with the following deviation from the agreed Study plan:

- the temperature and relative humidity recorded in the animal room were sometimes outside of the target ranges specified in the Study plan.

This minor deviation was not considered to have compromised the validity or integrity of the study.

3. RESULTS

The observations recorded during the study are presented in tables 1, 2 and 3.
The body weight is presented in table 4.

After a 3-minute exposure (one animal)
No cutaneous reactions were observed.
A grey coloration of the skin was noted from day 1 until day 4.

After a 1-hour exposure (one animal)
A grey coloration of the skin was noted from day 1 until day 4. This coloration could have masked a possible very slight erythema (grade 1) on day 1. No cutaneous reactions were observed from day 2 until day 4.

After a 4-hour exposure (three animals)
A grey coloration of the skin was noted in all the animals all over the observation period. This coloration could have masked a possible very slight or well-defined erythema (grade 1 or 2) from day 1 until day 2, 3 or 4.
A very slight erythema (grade 1) was noted in 1/3 animals on days 4 and 5. A dryness of the skin was noted in 2/3 animals between day 4 and day 7.

Due to the coloration of the skin, the mean scores over 24, 48 and 72 hours for each animal were not calculable for erythema. For edema, the mean scores over 24, 48 and 72 hours for each animal were 0.0, 0.0 and 0.0.
However, taking into account the possible erythema masked by the coloration, the maximal mean values over 24, 48 and 72 hours for erythema could be: 0.3, 1.0 and 1.3.

4. CONCLUSION

Under the experimental conditions of this study, when applied topically to rabbits, the test item [redacted] conclusions about its skin irritation potential.

However, taking into account the possible maximal mean values for erythema, the test item [redacted]

Table 1: 3-minute exposure - Cutaneous examinations and mean values of the scores recorded for the first animal (24, 48 and 72 hours)

Rabbit number	Dermal Irritation	Scores				Mean irritation score (1)
		1h D1	24h D2	48h D3	72h D4	
513 / 474	Erythema	0	0	0	0	0.0
	Edema	0	0	0	0	0.0
	Other	C	C	C	C	

(1) mean of scores on days 2, 3 and 4
h = hour
D = day
C = grey coloration of the skin

Table 2: 1-hour exposure - Cutaneous examinations and mean values of the scores recorded for the first animal (24, 48 and 72 hours)

Rabbit number	Dermal Irritation	Scores				Mean irritation score (1)
		1h D1	24h D2	48h D3	72h D4	
513 / 474	Erythema	C1	0	0	0	0.0
	Edema	0	0	0	0	0.0
	Other	*	C	C	C	

(1) mean of scores on days 2, 3 and 4
h = hour
D = day
* = none
C = grey coloration of the skin
C1 = grey coloration of the skin which could have masked a possible very slight erythema

Table 3: 4-hour exposure - Individual cutaneous examinations and mean values of the scores recorded for each animal (24, 48 and 72 hours)

Rabbit number	Dermal Irritation	Scores				Mean irritation score (1)
		1h D1	24h D2	48h D3	72h D4	
513 / 474	Erythema	C2	C1	0	0	(2)
	Edema	0	0	0	0	0.0
	Other	*	*	C	C	
483	Erythema	C1	C1	C1	C1	(2)
	Edema	0	0	0	0	0.0
	Other	*	*	*	*	
484	Erythema	C2	C2	C1	1	(2)
	Edema	0	0	0	0	0.0
	Other	*	*	*	C/S	

(1) mean of scores on days 2, 3 and 4
(2) = not calculable
h = hour
D = day
(+) = irritant according to E.E.C. criteria
(-) = non-irritant according to E.E.C. criteria
* = none
S = dryness of the skin
C = grey coloration of the skin
C1 = grey coloration of the skin which could have masked a possible very slight erythema
C2 = grey coloration of the skin which could have masked a possible well-defined erythema

Table 3 (continued)

Rabbit number	Dermal Irritation	Scores			
		D5	D6	D7	D8
513 / 474	Erythema	-	-	-	-
	Edema	-	-	-	-
	Other	-	-	-	-
483	Erythema	0	0	0	0
	Edema	0	0	0	0
	Other	C/S	C/S	C/S	C
484	Erythema	1	0	0	0
	Edema	0	0	0	0
	Other	C/S	C/S	C/S	C

D = day
S = dryness of the skin
C = grey coloration of the skin
- = cutaneous examination not performed

Table 4: Individual body weight (g)

Sex	Animals	Day of treatment	End of the observation period
Male	513 / 474	2607	2763
	483	2440	2560
	484	2351	2557
	M	2466	2627
	SD	130	118

M = mean
SD = standard deviation

[redacted]

APPENDICES

1. Test article description and analytical certificate

[redacted]

[redacted]

[redacted] DESCRIPTION

[redacted]

IDENTITY	
Test article name	[redacted]
Chemical name	
CAS number	
EINECS number	
Origin	
Batch number	
Arkema filing number	

PHYSICAL AND CHEMICAL PROPERTIES		
Appearance	:	black powder
Particule size	:	30 µm (approximately)
Specific Gravity	:	2,1 kg/m3 at 20°C
Autoignition temperature	:	> 400 °C (standard : NF EN 50281-2-1)
Solubility	:	in water : insoluble

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

See Safety Data Sheet.

STORAGE AND DISPOSAL		
Storage	:	Keep hermetically closed in a dry, cool and well-ventiled place .
Expiry date	:	June 2008
Disposal	:	Incineration

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[redacted]

[redacted]

DETERMINATION / *ITEM*	RESULTAT / *RESULT*	Référence de la méthode d'analyse / *Analysis reference*
Powder characteristics		
Ash content (%)	7.6%	ATG
Apparent density (kg/m³)	70	Weigh-in
[redacted]	[redacted]	[redacted]

Nom du responsable du laboratoire/ *Laboratory Director* :

Signature

[redacted]

2. Diet formula

Ref: 110

COMPLETE DIET

RABBIT BREEDING DIET

Appearance: 3 mm diameter granules

Conditioning: bags of 20 kgs

Daily portion: Rabbits 150 g, water *ad libitum*.

FORMULA %

Cereals	33.8
Grain biproducts and leguminous plants	48
Vegetable protein (soya bean meal, yeast)	14
Vitamin and mineral mixture	4.2

AVERAGE ANALYSIS %

Calorific value (Kcal/kg)	3100
Moisture	10
Proteins	15
Lipids	2.3
Carbohydrates (N.F.E.)	48.2
Fibre	17
Minerals (ash)	7.5

AMINO ACID VALUES (calculated in mg/kg)

Arginine	11300
Cystine	3400
Lysine	9300
Methionine	2800
Tryptophan	2400
Glycine	8700

FATTY ACID VALUES (calculated in mg/kg)

Palmitic acid	6400
Palmitoleic acid	0
Stearic acid	600
Oleic acid	6400
Linoleic acid	12100
Linolenic acid	2400

MINERALS (calculated in mg/kg)

	Nat. val.	CMV val.	Total
P	3600	2900	6500
Ca	4200	5800	10000
K	12000	0	12000
Na	400	2000	2400
Mg	2500	100	2600
Mn	50	40	90
Fe	150	150	300
Cu	Traces	15	15
Zn	30	45	75
Co	0.1	1.5	1.6
I	0.1	0	0.1
Cl	300	3000	3300

VITAMINS (calculated per kg)

	Nat. val.	CMV val.	Total
Vitamin A	Traces	10000 IU	10000 IU
Vitamin D3	0 IU	1000 IU	1000 IU
Vitamin B1	5 mg	0 mg	5 mg
Vitamin B2	4 mg	0 mg	4 mg
Vitamin B3	20 mg	0 mg	20 mg
Vitamin B6	1 mg	1 mg	2 mg
Vitamin B12	0 mg	0 mg	0 mg
Vitamin E	15 mg	25 mg	40 mg
Vitamin K3	0 mg	1 mg	1 mg
Vitamin PP	60 mg	5 mg	65 mg
Folic acid	0 mg	0 mg	0 mg
Biotin	0 mg	0 mg	0 mg
Choline	1000 mg	1000 mg	2000 mg

Available under quality "Control Ref.: 110"

SAFE, 7 rue Galliéni, Villemoisson, 91360 Epinay-sur-Orge
Tel: 01.69.04.03.57 - Fax : 01.69.04.81.97
(Ref. Doc. UAR: 2000)

[redacted] 28

3. CIT GLP certificate

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

GROUPE INTERMINISTERIEL DES PRODUITS CHIMIQUES

Paris, le - 9 JUIL. 2007

Objet : Evaluation de la conformité aux Bonnes Pratiques de Laboratoires (BPL) selon les directives 2004/9/CE et 2004/10/CE du 11 février 2004.

***Subject** : Assessment of compliance with Good Laboratory Practices (GLP) under the EC directives 2004/9 and 2004/10 of 11 February 2004.*

Consécutivement à votre engagement vis-à-vis du GIPC et du COFRAC et en application du décret n° 2006-1523 du 4 décembre 2006 concernant les bonnes pratiques de laboratoires et modifiant le décret n° 81-278 du 25 mars 1981 portant création d'un groupe interministériel des produits chimiques, je vous confirme que le GIPC, au vu des résultats du contrôle exercé par le Comité français d'accréditation (COFRAC) - Section Laboratoires a décidé pour votre installation du statut suivant :
Following your engagement vis-à-vis the GIPC and COFRAC and in application of the decree n° 2006-1523 of 4 December 2006 relating to the good laboratory practices and modifying the decree n° 81-278 of 25 March 1981 giving birth to an interministerial group of chemical products (GIPC), I confirm to you that the GIPC, given the results of the inspection realised by the French Committee of accreditation (COFRAC) – Laboratory Section has taken the following decision relating to your installation

Respect des principes de BPL
Respect of the GLP principles

Domaines de reconnaissance:
1 - essais physico-chimiques
2 - études de toxicité
3 - études de mutagénicité
4 - études écotoxicologiques sur les organismes aquatiques et terrestres
8 - méthodes de chimie analytique et clinique

Areas of expertise :
1 = Physico-chemical testing
2 = Toxicity studies
3 = Mutagenicity studies
4 = Environmental toxicity studies on aquatic or terrestrial organisms
8 = Analytical and clinical chemistry

Date d'inspection : 7-8 mars 2007
Date of inspection : 7-8 mars 2007

Inspection de renouvellement (i.r)
Renewal inspection (i.r)

Date de décision du GIPC : 29 juin 2007
Date of GIPC decision: 29 juin 2007

Date de prise d'effet : 8 mars 2007
Date of implementation: 8 mars 2007

Année de première conformité : 1989
Year of the first conformity: 1989

Durée de validité: 18 mois
Time of validity: 18 months

Le Président,

Pierre CREYSSEL
Conseiller d'Etat h

CENTRE INTERNATIONAL DE TOXICOLOGIE
(CIT)
MISEREY – BP 563
27005 EVREUX CEDEX

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
P-09-185 Modified consent order		10-18-13

COMMENTS:

DOES NOT CONTAIN CBI

V-2. 4/1/11
RJA 4/1/11

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

OFFICE OF POLLUTION PREVENTION AND TOXICS

REGULATION OF A NEW CHEMICAL SUBSTANCE

PENDING DEVELOPMENT OF INFORMATION

In the matter of: [redacted]

Premanufacture Notice Number:

P-09-0188

CONTAINS NO CBI

RECEIVED
OPPT CBIC
2013 OCT 18 PM 3:52

[redacted]

DOES NOT CONTAIN NATIONAL SECURITY INFORMATION (E.O.12065)

Modified Consent Order and Determinations Supporting the Modified Consent Order

TABLE OF CONTENTS

PREAMBLE

This is a modified Consent Order of the original Consent Order, which became effective on April 22, 2010. The purpose of this Modified Consent Order is to 1) modify the terms of the Distribution Section of the Toxic Substances Control Act (TSCA) section 5(e) Consent Order between the U.S. Environmental Protection Agency (EPA) and [redacted] (the "Company"); and 2) Extend the time allowed to generate certain material characterization data which was triggered under the original Consent Order.

The Modifications are necessary to allow, prior to promulgation of a final Significant New Use Rule, for distribution in commerce by Processors who have signed a Consent Order for Processor of the multi-walled carbon nanotubes in a liquid polymer form for use in [redacted], one of the original specific uses in the PMN. Additionally, the Company has relinquished certain claims of Confidential Business Information (CBI) on the specific chemical identify of their PMN substance, namely, the Agency may now refer to the PMN substance as multi-walled carbon nanotubes ("MWCNTs"). The Company maintains their CBI claims on the specific material characteristics of their MWCNTs such as, but not limited to inner diameter and length. Due to difficulties in developing appropriate protocols on these particular nanoscale materials and finding a laboratory, the Company requested, and the Agency has granted, an extension on the time period to generate certain triggered testing for material characterization.

I INTRODUCTION

Under the authority of § 5(e) of the Toxic Substance Control Act ("TSCA") (15 U.S.C. 2604(e)), the Environmental Protection Agency ("EPA" or "the Agency") issues the attached

Order, regarding premanufacture notice ("PMN") P-09-0188 for the chemical substance, multi-wall carbon nanotubes ("MWCNTs") (the "PMN substance"), submitted by [redacted] ("the Company"), to take effect upon expiration of the PMN review period. The Company submitted the PMN to EPA pursuant to section 5(a)(1) of TSCA and 40 CFR Part 720.

Under § 15 of TSCA, it is unlawful for any person to fail or refuse to comply with any provision of § 5 or any order issued under § 5. Violators may be subject to various penalties and to both criminal and civil liability pursuant to § 16, and to specific enforcement and seizure pursuant to § 17. In addition, chemical substances subject to an Order issued under § 5 of TSCA, such as this one, are subject to the § 12(b) export notice requirement.

II. SUMMARY OF TERMS OF THE ORDER

The Modified Consent Order for this PMN substance requires the Company to:

1. submit to EPA certain toxicity testing on the powder form of the PMN substance before exceeding either the specified production volume or a specified time period;
2. before exceeding a specified time period, submit to EPA certain material and physical-chemical data on the PMN substance in the powder form;
3. require workers to wear personal protective equipment including gloves, chemical protective clothing and goggles in the work area whenever reasonably likely to be dermally exposed to the PMN substance in the work area;
4. whenever workers are reasonably likely to be exposed to the PMN substance by inhalation require workers to wear a NIOSH-certified air-purifying, tight-fitting full-face respirator equipped with N-100, P-100, or R-100 filter; a NIOSH-certified powered air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of

an APF of 1,000; a NIOSH-certified continuous flow supplied air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of an APF of 1,000; or a NIOSH-certified continuous flow supplied air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of an APF of 1,000, except when the PMN substance is in the following forms:

- in a liquid polymer form with a concentration of the PMN substance equal to or below 7%, provided the activity does not generate a vapor, mist, or aerosol; or
- embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30% provided the activity does not generate a dust;

5. use and distribute the PMN substance only for the following uses specified in the PMN: [redacted];
6. not use the PMN substance for commercial or consumer use, or in a consumer product (quantities of PMN substance that are completely reacted, cured, or embedded as described in the Order may be used for commercial or consumer use, or in a consumer product);
7. not manufacture the PMN substance in the United States;
8. provide the U.S. EPA with a 1 g sample of the PMN substance upon request by EPA;
9. distribute the PMN substance only to a person who agrees to follow the same restrictions applicable to the company (except the testing requirements) and to not further distribute the PMN substance until after it has been completely reacted (cured), incorporated into a

polymer matrix that itself has been reacted (cured), or embedded into a solid polymer form with a concentration of the PMN substance equal to or below 30%;

10. not release the PMN substance to the waters of the United States except where the PMN substance is embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30%; and
11. maintain relevant records.

A Consent Order for Processors is attached to extend these requirements to any Processor.

In summary, the "Scope of Applicability and Exemption" section of the Order exempts the following:

1. quantities of the PMN substance that have been completely reacted (cured), incorporated or embedded into a polymer matrix that itself has been reacted (cured), or embedded in a permanent solid polymer form with a concentration of the PMN substance equal to or below 30% that will not undergo further processing except for mechanical processing. These exemptions do not apply beyond the uses that are specifically authorized by the Order in the Manufacturing, and Processing and Use sections, but do allow use for commercial or consumer use, or in a consumer product.
2. quantities designated solely for export before the Company commences import of the PMN substance for use within the United States;
3. research & development ("R&D");
4. the PMN substance as a byproduct without separate commercial intent; and
5. the PMN substance in a substance, mixture, or article with no separate commercial purpose.

III. CONTENTS OF PMN

By signing this Order, the Company represents that it has carefully reviewed this document and hereby agrees that all information herein that is claimed as confidential by the Company (per section 14 of TSCA, 40 CFR Part 720 Subpart E, and 40 CFR Part 2) is correctly identified within brackets and that any information that is not bracketed is not claimed as confidential. To make this document available for public viewing, EPA will remove only the information contained within the brackets.

Confidential Business Information Claims (Bracketed in the Preamble and Order):

Company name, specific chemical identity, production volume, physical properties, material characterization, precursor substances, typical composition, process information, impurities, use, byproducts, and worker/occupational exposure.

Chemical Identity:

Specific identity: [redacted].

Generic identity: multi-walled carbon nanotubes.

Chemical Form: The Notice identifies four forms of the PMN substance:

1. **Powdered – [redacted]**
2. **Liquid polymer form with a concentration of the PMN substance up to [redacted] ("liquid polymer form"): [redacted]**
3. **Solid polymer form with a concentration of the PMN substance up to [redacted] ("solid polymer form"): [redacted]**

[redacted]

4. The PMN also describes the final end use form of the PMN substance. For this Modified Consent Order, this form is described as being completely reacted (cured), incorporated or embedded into a polymer matrix that itself has been reacted (cured), or embedded in a permanent solid polymer form with a concentration of the PMN substance equal to or below 30% that will not undergo further processing, except for mechanical processing (**"PMN substance that is reacted, cured, or embedded in a permanent solid polymer"**).

Use:

Specific: [redacted]

Generic: electric conductive filler to replace conventional material such as carbon black, or carbon fiber in matrices such as polymer resin for conductive applications.

Maximum 12-Month Production Volume: [redacted] kg/yr; Import only.

Test Data Submitted with PMN:

- Toxicity to bacteria;
- Chromosomal aberrations in cultured human cells;
- Skin sensitization in mouse lymph node assay;
- Acute dermal toxicity in the rat;
- Acute oral toxicity in the rat;
- Acute eye irritation in rabbits;
- Acute dermal irritation in rabbits;
- Intratracheal insertion of single-walled carbon nanotubes produced inflammatory reactions in mouse and rat lungs, with fibrogenic responses (MSDS);
- Study of the granulometry of the carbon nanotube powder;
- Coating with a polystyrene polymer protects against respiratory toxicity of carbon nanotubes *in vitro* and *in vivo* in mice;
- *In vitro* mammalian cell gene mutation in L5178Y TK+/- mouse lymphoma cells;
- Adverse effects of industrial multiwalled carbon nanotubes on human pulmonary cells;
- Degradation and release of polymer nanocomposites exposed to ultraviolet radiation;
- Baseline carbon nanotubes air sampling conducted at the [redacted];
- Absence of carcinogenic response to MWCNTs in a 2-year bioassay in the peritoneal cavity of the rat on an analogous substance to the PMN;
- Detection of [redacted] carbon nanotubes in water by UV-Vis spectrometry to determine [redacted] transferability from liquids and pastes to water; and
- Detection of respirable nanoparticles released from a viscous paste consisting of [redacted] MWCNTs following vigorous manipulation.

IV. EPA'S ASSESSMENT OF RISK

The following are EPA's predictions regarding the probable toxicity, human exposure and environmental release of the PMN substance, based on the information currently available to the Agency.

Human Health Effects Summary:

Absorption is expected to be poor via all routes for the manufactured substance, based on test data for chemicals with similar molecular structures and chemicals with similar physical/chemical properties. Data on the PMN substance and other analogous substances

indicate the potential for generation of increased amounts of respirable or absorbable particles during processing and use of nanoscale materials. Much more evaluation is needed to determine the toxicity of nanoscale materials for all routes of exposure. There are concerns for lung effects, based on the EPA Respirable, Poorly Soluble Particulates chemical category. See www.epa.gov/oppt/newchems/pubs/cat02.htm#Respirable. Based on test data for analogous chemicals there are concerns for pulmonary toxicity, fibrosis, carcinogenicity, mutagenicity, and immunotoxicity of the PMN substance. There are also data suggesting that pulmonary deposition of some nanoscale materials, including carbon nanotubes in the agglomerated form, may induce cardiovascular toxicity when these nanoscale materials are inhaled. The major health concerns are for potential pulmonary toxicity, fibrosis and cancer to workers exposed via inhalation. The PMN substance as manufactured tested negative for skin sensitization in the Local Lymph Node Assay (LLNA) and was slightly irritating in an acute dermal irritation study in rabbits. Based on the uncertainty of the characterization and exposure of nanoscale materials in general, there may be additional potential for translocation across the dermis and effects on target organs.

Environmental Effects Summary:

Toxicity from carbon nano[redacted] ([redacted]) exposures has been reported in many aquatic species at concentrations much higher than any estimated solubility limits. Even though CNTs are not appreciably water soluble as manufactured, aqueous CNT suspensions can be easily made through reaction with strong acids, ozone, or dispersing agents. Recent laboratory research shows that [redacted] combine with dissolved organic matter (DOM) to form stable aqueous suspensions. No studies on CNTs are available in which a broad range of production methods,

sources, purification, functionalization, etc. were investigated. EPA expects that some fraction of the CNTs, if released into the environment, will eventually become suspended in water. Sublethal effects have been noted for single-walled carbon nanotubes (SWCNT) in fish at levels as low as 100 ppb. Noted effects included respiratory stress, ventilation rate, gill mucus secretion, gill damage, and aggressive behaviors. Liver cell injuries were also readily apparent at these exposure levels and suggest the possibility of liver tumor formation over longer exposure periods. This response is also notable because effects were seen in cells closest to blood vessels, suggesting transport of respired or ingested SWCNTs via the blood stream. Some effects in the gut lumen were also observed at these exposure levels. Further studies need to be conducted before EPA can determine a concentration of concern. Such studies must measure actual concentrations of carbon nanotubes and control for the effects of contaminants, solvents, and physical factors such as blockage of gills or intestines. Before such testing is conducted, advanced fate testing would be necessary to ascertain what substance is likely to present the highest environmentally relevant concentrations.

Exposure and Environmental Release Summary:

	Manufacture	**Processing**	**Use**	**Consumer**
# Sites	Imported	[redacted]	[redacted]	N/A
Workers (#/site)	Imported	[redacted]	[redacted]	N/A
Exposure (days/year)	Imported	[redacted]	[redacted]	None expected

	Manufacture	Processing	Use	Consumer
Inhalation Exposure (mg/day)	Imported	[redacted]	[redacted]	None expected
Dermal Exposure (mg/day)	Imported	[redacted]	[redacted]	None expected
Drinking Water Exposure (mg/kg/day)	Imported	[redacted]	[redacted]	None expected
Releases to all environmental media (days/year)	Imported	[redacted] days	[redacted] days	None expected
Release to Water (kg/day)	Imported	[redacted]	[redacted]	None expected
Fugitive Air Exposure (mg/kg/day)	Imported	[redacted]	[redacted]	None expected

Risk to Workers: The PMN substance may present a risk to workers exposed to the PMN substance via inhalation. In the table above, the worst case worker inhalation value is [redacted] during processing. As the PMN substance is manufactured, 1% of the particles are expected to be in the respirable size, though test data included with the PMN

suggest that this percentage is expected to increase as the PMN substance is handled. Previous similar cases have predicted occupational exposures as high as 0.05 mg/m^3 for respirable particles. Therefore, there is a concern for pulmonary toxicity, fibrosis and cancer and a potential for cardiovascular effects to workers exposed to the PMN via the inhalation route. To mitigate potential health effects via the inhalation route of exposure, the Order requires respiratory protection for the powdered form of the PMN substance and when a dust, vapor, mist, or aerosol containing the PMN substance is generated. EPA believes the PMN substance as manufactured presents a low risk to workers exposed to the PMN substance dermally, but does not have enough information to evaluate the risks when the PMN substance is handled. To mitigate potential health effects via the dermal route of exposure, the Order requires varying degrees of dermal protection based on the form of the PMN substance.

Risk to general population: There is potential for exposure of the general population and the environment from landfill releases. Human ingestion may result from landfill releases.

Environmental Risk: The amount of PMN substance expected to be released into the environment, in the absence of site-specific risk management practices described in the notice, would lead to surface water concentrations that exceeded environmental toxicities identified by EPA. Therefore, the attached Order prohibits releases of the PMN substance to surface water except for the solid polymer form with a concentration of the PMN substance equal to or below 30%.

V. EPA'S CONCLUSIONS OF LAW

The following findings constitute the basis of the Modified Consent Order:

(a) EPA is unable to determine the potential for effects to human health and the environment from exposure to the PMN substance. EPA therefore concludes, pursuant to § 5(e)(1)(A)(i) of TSCA, that the information available to the Agency is insufficient to permit a reasoned evaluation of the human health and environmental effects of the PMN substance.

(b) In light of the potential risk to human health and the environment posed by the uncontrolled manufacture, import, processing, distribution in commerce, use, and disposal of the PMN substance, EPA has concluded, pursuant to § 5(e)(1)(A)(ii)(I) of TSCA, that uncontrolled manufacture, import, processing, distribution in commerce, use, and disposal of the PMN substance may present an unreasonable risk of injury to human health and the environment.

VI. INFORMATION REQUIRED TO EVALUATE HEALTH EFFECTS

Triggered Testing. The Order prohibits the Company from exceeding specified time periods or production volumes unless the Company submits the information described in the Testing section of this Order in accordance with the conditions specified in the Testing section. The Order's restrictions on manufacture, import, processing, distribution in commerce, use, release to water, and disposal of the PMN substances will remain in effect until the Order is modified or revoked by EPA based on submission of that or other relevant information. EPA encourages the Company to develop additional health effects testing in coordination with other manufacturers of carbon nanotubes. This can be done under the in-depth portion of EPA's Nanoscale Materials Stewardship Program or through independent testing. EPA is willing to facilitate the process in

coordination with other ongoing health effects testing for the PMN substances nationally and internationally.

Pended Testing. The following additional information would be required to evaluate the following effects which may be caused by the PMN substance:

Environmental Exposures

The Company may submit the following environmental exposure data on a representative set of liquid polymer forms of the PMN substance.(EPA identified [redacted] in the PMN). The Company may propose alternative methods, guidelines, or representative sets subject to EPA's approval.

Characteristic or Property	**Guideline or method**
Release of MWCNTs after landfill disposal	EPA Method 1320: Multiple Extraction Procedure to determine the fraction of MWCNTs released during the leaching that the liquid polymer forms will undergo from repetitive precipitation of acid rain. Method 1320 uses EPA Method 1310B: Extraction Procedure (EP) Toxicity Test Method and Structural Integrity Test as the basis for the multiple extraction method. Chapters 3 and 4 cited in Section 7.17 of Method 1310B refer to chapters in the SW-846 "Test Methods for Evaluating Solid Waste, Physical/Chemical Methods". However, instead of using these analyses methods, the analysis of MWCNTs in the extracts should be performed using EPA Method 100.1: Analytical Method for Determination of Asbestos Fibers in Water, which has an analytical sensitivity of approximately 3.3 μg/L for a MWCNT that is 10 nm [redacted]. An allowable alternative analytical approach would be to use Raman spectroscopy (see Liu et al., PNAS, 2008, 105(5), 1410-1415).

Characteristic or Property	**Guideline or method**
Release of MWCNTs during the burning of liquid polymer forms	Consult ASTM E1354-09: Standard Test Method for Heat and Visible Smoke Release Rates for Materials and Products Using an Oxygen Consumption Calorimeter as the basis for this test. For example, this test method was used to determine the flammability of polyamide 11 and 12 nanocomposites (see Lao et al., J. Comp. Mat. 2009, 43, 1803-1818). Given that the airborne fraction of MWCNTs is of interest, the ASTM E1354-09 test would have to be modified so that samples of the off-gas could be collected and analyzed for MWCNT content. For the analytical method, consider using methods developed for airborne asbestos fibers found in Appendix A to Subpart E–Interim Transmission Electron Microscopy Analytical Methods found in 40 CFR Part 763. [redacted] may want to consult with Dr. Marc R. Nyden, Building and Fire Research Laboratory, National Institute of Standards and Technology, Gaithersburg, MD.
Release of MWCNTs from after exposure of liquid polymer forms to sunlight	Polymeric resins are known to degrade after exposure to sunlight (see Polymer Photodegradation: Mechanisms and Experimental Methods, J.F Rabek, Chapman and Hall, London UK, 1995). Thus, if the MWCNT containing resins were exposed to sunlight, they are expected to degrade and release free MWCNTs into the environment (see Nguyen et al., Degradation of Nanofiller Release of Polymer Nanocomposites Exposed to Ultraviolet Radiation, NIST, Gaithersburg, MD). ASTM D2565-99(2008) Standard Practice for Xenon-Arc Exposure of Plastics Intended for Outdoor Applications should be consulted.

The Company may submit the following environmental exposure data on a representative set of solid polymer forms of the PMN substance (EPA identified [redacted] in the PMN). The Company may propose alternative methods, guidelines, or representative sets subject to EPA's approval.

Characteristic or Property	**Guideline or method**
Release of MWCNTs after landfill disposal	EPA Method 1320: Multiple Extraction Procedure to determine the fraction of MWCNTs released during the leaching that the solid polymer forms will undergo from repetitive precipitation of acid rain. Method 1320 uses EPA Method 1310B: Extraction Procedure (EP) Toxicity Test Method and Structural Integrity Test as the basis for the multiple extraction method. Chapters 3 and 4 cited in Section 7.17 of Method 1310B refer to chapters in the SW-846 "Test Methods for Evaluating Solid Waste, Physical/Chemical Methods". However, instead of using these analyses methods, the analysis of MWCNTs in the extracts should be performed using EPA Method 100.1: Analytical Method for Determination of Asbestos Fibers in Water, which has an analytical sensitivity of approximately 3.3 µg/L for a MWCNT that is [redacted]. An alternative analytical approach would be to use Raman spectroscopy (see Liu et al., PNAS, 2008, 105(5), 1410-1415).
Release of MWCNTs during the burning of solid polymer resins	Consult ASTM E1354-09: Standard Test Method for Heat and Visible Smoke Release Rates for Materials and Products Using an Oxygen Consumption Calorimeter as the basis for this test. For example, this test method was used to determine the flammability of polyamide 11 and 12 nanocomposites (see Lao et al., J. Comp. Mat. 2009, 43, 1803-1818). Given that the airborne fraction of MWCNTs is of interest, the ASTM E1354-09 test would have to be modified so that samples of the off-gas could be collected and analyzed for

	MWCNT content. For the analytical method, consider using methods developed for airborne [redacted]. [redacted] may want to consult with Dr. Marc R. Nyden, Building and Fire Research Laboratory, National Institute of Standards and Technology, Gaithersburg, MD.
Characteristic or Property	**Guideline or method**
Release of MWCNTs from after Exposure of solid polymer forms to sunlight	Polymeric resins are known to degrade after exposure to sunlight (see Polymer Photodegradation: Mechanisms and Experimental Methods, J.F Rabek, Chapman and Hall, London UK, 1995). Thus, if the MWCNT containing polymer forms were exposed to sunlight, they are expected to degrade and release free MWCNTs into the environment (see Nguyen et al., Degradation of Nanofiller Release of Polymer Nanocomposites Exposed to Ultraviolet Radiation, NIST, Gaithersburg, MD). ASTM D2565-99(2008) Standard Practice for Xenon-Arc Exposure of Plastics Intended for Outdoor Applications should be consulted.
Release of MWCNTs during solid polymer form shipping and use	[redacted] which are resin based composites ([redacted]3]). Presumably the MWCNTs would also be released from the solid resins during mechanical agitation of the solid resins. Mechanical agitation could potentially occur during shipping and transfer of the [redacted] containing solid resins. [redacted] should develop a testing protocol to determine if MWCNTs are released from solid resins during mechanical agitation. While no standard methods exist, [redacted] should consider developing a simple short-term test consisting of placing the solid polymer forms in a standard rock tumbler and determining the amount of free MWCNTs after a period of 1, 5, 15,

	and 30 days to screen for significant release of MWCNTs from the solid polymer forms.

The Order does not require submission of the above pended testing at any specified time or production volume. However, the Order's restrictions on manufacture, import, processing, distribution in commerce, use, and disposal of the PMN substance will remain in effect until the Order is modified or revoked by EPA based on submission of that or other relevant information.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

[redacted]

MODIFIED CONSENT ORDER

I. SCOPE OF APPLICABILITY AND EXEMPTIONS

(a) Scope. The requirements of this Order apply to all commercial manufacturing, processing, distribution in commerce, use and disposal, in the United States, of the chemical substance multi-walled carbon nanotubes ("MWCNTs") (the "PMN substance") by [redacted].] ("the Company"), except to the extent that those activities are exempted by paragraph (b). The Original Consent Order, which became effective on April 22, 2010, will be superseded by the Modified Consent Order once the Modified Consent Order becomes effective.

(b) Exemptions. Manufacturing, processing, distribution in commerce, use and disposal of the PMN substance are exempt from the requirements of this Order (except the requirements in the Recordkeeping and Successor Liability Upon Transfer Of Modified Consent Order sections) only

to the extent that (1) these activities are conducted in full compliance with all applicable requirements of the following exemptions, and (2) such compliance is documented by appropriate recordkeeping as required in the Recordkeeping section of this Order.

(1) Completely Reacted, Cured, or Embedded. If quantities of the PMN substance (A) are used solely for the uses authorized in paragraph (c) of the Manufacturing section and by paragraphs (a) and (b), of the Processing/Use section of this Order; and (B) those quantities have been (i) completely reacted (cured); (ii) incorporated or embedded into a polymer matrix that itself has been reacted (cured); (iii) or embedded in a permanent solid polymer form with a concentration of the PMN substance equal to or below 30% that is not intended to undergo further processing except for mechanical processing; then the other requirements of this Order do not apply.

(2) Export. Until the Company begins commercial manufacture of the PMN substance for use in the United States, the requirements of this Order do not apply to manufacture, processing or distribution in commerce of the PMN substance solely for export in accordance with TSCA §12(a) and (b), 40 CFR 720.3(s) and 40 CFR Part 707. However, once the Company begins to manufacture the PMN substance for use in the United States, no further activities by the Company involving the PMN substance are exempt as "solely for export" even if some amounts of the PMN substance are later exported. At that point, the requirements of this Order apply to all activities associated with the PMN substance while in the territory of the United States. Prior to leaving U.S. territory, even those quantities or batches of the PMN substance that are destined for export are subject to terms of the Order, and count towards any production volume test triggers in the Testing section of this Order.

(3) Research & Development ("R&D"). The requirements of this Order do not apply to

manufacturing, processing, distribution in commerce, use and disposal of the PMN substance in small quantities solely for research and development in accordance with TSCA §5(h)(3), 40 CFR 720.3(cc), and 40 CFR 720.36.

(4) Byproducts. The requirements of this Order do not apply to the PMN substance when it is produced, without separate commercial intent, only as "byproducts" as defined at 40 CFR 720.3(d) and in compliance with 40 CFR 720.30(g).

(5) No Separate Commercial Purpose. The requirements of this Order do not apply to the PMN substance when it is manufactured, pursuant to any of the exemptions in 40 CFR 720.30(h), with no commercial purpose separate from the substance, mixture, or article of which it is a part.

(c) Automatic Sunset. If the Company has obtained for the PMN substance a Test Market Exemption ("TME") under TSCA §5(h)(1) and 40 CFR 720.38 or a Low Volume Exemption ("LVE") or Low Release and Exposure Exemption ("LoREx") under TSCA §5(h)(4) and 40 CFR 723.50(c)(1) and (2) respectively, any such exemption is automatically rendered null and void as of the effective date of this Modified Consent Order.

II. TERMS OF MANUFACTURE, IMPORT, PROCESSING, DISTRIBUTION IN COMMERCE, USE, AND DISPOSAL PENDING SUBMISSION AND EVALUATION OF INFORMATION

PROHIBITION

The Company is prohibited from manufacturing, importing, processing, distributing in commerce, using, or disposing of the PMN substance in the United States, for any nonexempt commercial purpose, pending the development of information necessary for a reasoned evaluation

of the human health and environmental effects of the substance, and the completion of EPA's review of, and regulatory action based on, that information, except in accordance with the conditions described in this Order.

TESTING

(a) Section 8(e) Reporting. Reports of information on the PMN substance which reasonably supports the conclusion that the PMN substance presents a substantial risk of injury to health or the environment and which is required to be reported under TSCA section 8(e) shall reference the appropriate PMN identification number for this substance and contain a statement that the substance is subject to this Modified Consent Order. Additional information regarding section 8(e) reporting requirements can be found at www.epa.gov/oppt/tsca8e.

(b) Notice of Study Scheduling. The Company shall notify, in writing, the EPA Laboratory Data Integrity Branch (2225A), Office of Enforcement and Compliance Assurance, U.S. Environmental Protection Agency, 1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460, of the following information within 10 days of scheduling any study required to be performed pursuant to this Order, or within 15 days after the effective date of this Order, whichever is later:

(1) The date when the study is scheduled to commence;

(2) The name and address of the laboratory which will conduct the study;

(3) The name and telephone number of a person at the Company or the laboratory whom EPA may contact regarding the study; and

(4) The appropriate PMN identification number for the substance and a statement that the

substance is subject to this Modified Consent Order.

(c) Good Laboratory Practice Standards and Test Protocols. Each study required to be performed pursuant to this Order must be conducted according to TSCA Good Laboratory Practice Standards at 40 CFR Part 792 and using methodologies generally accepted in the relevant scientific community at the time the study is initiated. Before starting to conduct any such study, the Company must obtain approval of test protocols from EPA by submitting written protocols. EPA will respond to the Company within 4 weeks of receiving the written protocols. Published test guidelines specified in paragraph (d) provide general guidance for development of test protocols, but are not themselves acceptable protocols. Approval of the test protocol does not mean pre-acceptance of test results.

(d) Triggered Testing Requirements.

The Company is prohibited from manufacturing or importing the PMN substance for non-exempt purposes beyond either of the following time or aggregate manufacture and import volume limits of the non-exempt PMN substance (collectively "the production limit") unless the Company conducts the following tests on the PMN substance and submits all final reports and underlying data in accordance with the conditions specified in this Testing section.

(1) Toxicity Tests. The production limit for these tests shall be calculated starting two years after expiration of the PMN review period.

Production Limit	Test	Guideline
[redacted] or [redacted] kg, whichever comes first	90-day inhalation toxicity test, with a post-exposure observation period of up to 3 months, bronchoalveolar lavage fluid (BALF) analysis, aggregation/agglomeration state, shape, size/size particle distribution and surface properties of materials as-administered, aggregation/ agglomeration state, shape, size/size particle distribution and surface properties of materials of the delivered materials after administration, determination of cardiovascular toxicity, heart histopathology, and data on pulmonary deposition.	OPPTS 870.3465

(2) Material Characterization and Physical-Chemical Properties. The Company must submit the following material characterization data on the PMN substance in the powdered form (including data summaries and procedures), and is strongly encouraged to send in proposed procedures before conducting the studies to allow EPA review. Description of the physical-chemical properties of the material tested and material characterization tests should take into consideration the characterizations identified in the Guidance Manual for Sponsors of the OECD Sponsorship Programme for the Testing of Manufactured Nanomaterials. These tests shall be due 18 months after expiration of the PMN review period. The Company may propose alternative methods or guidelines subject to EPA's approval.

Characteristic or Property	Guideline or method
[redacted]	Transmission-electron microscopy (TEM)
[redacted]	Scanning electron microscopy (SEM) and TEM
[redacted]	X-ray diffraction (XRD)
[redacted]	SEM & TEM
[redacted]	XRD
[redacted]	XRD
Particle sizes of catalyst used in the manf. of the nano[redacted]	Vendor specifications
Particle shape	Optical microscopy and surface area measurements
Particle size (average and distribution)	Optical microscopy and surface area measurements
Particle surface to volume ratio	Optical microscopy and surface area measurements
Agglomeration	Optical microscopy and surface area measurements
Particle surface area measurement	Optical microscopy and surface area measurements
Dustiness test	Deutsches Institut für Nörmung ("DIN") EN 15051 method

(e) Test Reports. The Company shall: (1) conduct each study in good faith, with due care, and in a scientifically valid manner; (2) promptly furnish to EPA the results of any interim phase of each study; and (3) submit, in triplicate (with an additional sanitized copy, if confidential business information is involved), the final report of each study and all underlying data ("the report and data") to EPA no later than 14 weeks prior to exceeding the applicable production limit. The final report shall contain the contents specified in 40 CFR 792.185. Underlying data shall be submitted to EPA in accordance with the applicable "Reporting", "Data and Reporting", and "Test Report" subparagraphs in the applicable test guidelines. However, for purposes of this Modified Consent

Order, the word "should" in those subparagraphs shall be interpreted to mean "shall" to make clear that the submission of such information is mandatory. EPA will not require the submission of raw data such as slides and laboratory notebooks unless if EPA finds, on the basis of professional judgment, that an adequate evaluation of the study cannot take place in the absence of these items.

(f) Testing Waivers. The Company is not required to conduct a study specified in paragraph (d) of this Testing section if notified in writing by EPA that it is unnecessary to conduct that study.

(g) Equivocal Data. If EPA finds that the data generated by a study are scientifically equivocal, the Company may continue to manufacture and import the PMN substance beyond the applicable production limit. To seek relief from any other restrictions of this Order, the Company may make a second attempt to obtain unequivocal data by reconducting the study under the conditions specified in paragraphs (b), (c), and (e)(1) and (2). The testing requirements may be modified, as necessary to permit a reasoned evaluation of the risks presented by the PMN substance, only by mutual consent of EPA and the Company.

(h) EPA Determination of Invalid Data.

(1) Except as described in subparagraph (h)(2) of this Section, if, within 6 weeks of EPA's receipt of a test report and data, the Company receives written notice that EPA finds that the data generated by a study are scientifically invalid, the Company is prohibited from further manufacture and import of the PMN substance beyond the applicable production limit.

(2) The Company may continue to manufacture and import the PMN substance beyond the applicable production limit only if so notified, in writing, by EPA in response to the Company's

compliance with either of the following subparagraphs (h)(2)(i) or (h)(2)(ii).

(i) The Company may reconduct the study in compliance with paragraphs (b), (c), and (e)(1) and (2). If there is sufficient time to reconduct the study and submit the report and data to EPA at least 14 weeks before exceeding the production limit as required by subparagraph (e)(3) of this Section, the Company shall comply with subparagraph (e)(3) of this Section. If there is insufficient time for the Company to comply with subparagraph (f)(3) of this Section, the Company may exceed the production limit and shall submit the report and data in triplicate to EPA within a reasonable period of time, all as specified by EPA in the notice described in subparagraph (h)(1) of this Section. EPA will respond to the Company, in writing, within 6 weeks of receiving the Company's report and data.

(ii) The Company may, within 4 weeks of receiving from EPA the notice described in subparagraph (h)(1) of this Section, submit to EPA a written report refuting EPA's finding. EPA will respond to the Company, in writing, within 4 weeks of receiving the Company's report.

(i) Company Determination of Invalid Data.

(1)Except as described in subparagraph (i)(2) of this Section, if the Company becomes aware that circumstances clearly beyond the control of the Company or laboratory will prevent, or have prevented, development of scientifically valid data under the conditions specified in paragraphs (c) and (e), the Company remains prohibited from further manufacture and import of the PMN substance beyond the applicable production limit.

(2) The Company may submit to EPA, within 2 weeks of first becoming aware of such circumstances, a written statement explaining why circumstances clearly beyond the control of the Company or laboratory will cause or have caused development of scientifically invalid data. EPA

will notify the Company of its response, in writing, within 4 weeks of receiving the Company's report. EPA's written response may either:

(i) allow the Company to continue to manufacture and import the PMN substance beyond the applicable production limit, or

(ii) require the Company to continue to conduct, or to reconduct, the study in compliance with paragraphs (b), (c), and (e)(1) and (2). If there is sufficient time to conduct or reconduct the study and submit the report and data to EPA at least 14 weeks before exceeding the production limit as required by subparagraph (e)(3) of this Section, the Company shall comply with subparagraph (e)(3) of this Section. If there is insufficient time for the Company to comply with subparagraph (e)(3) of this Section, the Company may exceed the production limit and shall submit the report and data in triplicate to EPA within a reasonable period of time, all as specified by EPA in the notice described in subparagraph (i)(2) of this Section. EPA will respond to the Company, in writing, within 6 weeks of receiving the Company's report and data, as to whether the Company may continue to manufacture and import beyond the applicable production limit.

(j) Unreasonable Risk.

(1) EPA may notify the Company in writing that EPA finds that the data generated by a study are scientifically valid and unequivocal and indicate that, despite the terms of this Order, the PMN substance will or may present an unreasonable risk of injury to human health or the environment. EPA's notice may specify that the Company undertake certain actions concerning further testing, manufacture, import, processing, distribution, use and/or disposal of the PMN substance to mitigate exposures to or to better characterize the risks presented by the PMN substance. Within 2 weeks from receipt of such a notice, the Company must cease all

manufacture, import, processing, distribution, use and disposal of the PMN substance, unless either:

(2) within 2 weeks from receipt of the notice described in subparagraph (j)(1) of this Section, the Company complies with such requirements as EPA's notice specifies; or

(3) within 4 weeks from receipt of the notice described in subparagraph (j)(1) of this Section, the Company submits to EPA a written report refuting EPA's finding and/or the appropriateness of any additional requirements imposed by EPA. The Company may continue to manufacture, import, process, distribute, use and dispose of the PMN substance in accordance with the terms of this Order pending EPA's response to the Company's written report. EPA will respond to the Company, in writing, within 4 weeks of receiving the Company's report. Within 2 weeks of receipt of EPA's written response, the Company shall comply with any requirements imposed by EPA's response or cease all manufacture, import, processing, distribution, use and disposal of the PMN substance.

(k) Other Requirements. Regardless of the satisfaction of any other conditions in this Testing section, the Company must continue to obey all the terms of this Modified Consent Order until otherwise notified in writing by EPA. The Company may, based upon submitted test data or other relevant information, petition EPA to modify or revoke provisions of this Modified Consent Order pursuant to Part VI of this Modified Consent Order.

PROTECTION IN THE WORKPLACE

(a) Establishment of Program. During manufacturing, processing, and use of the non-exempt PMN substance at any site controlled by the Company (including any associated packaging and

storage and during any cleaning or maintenance of equipment associated with the PMN substance), the Company must establish a program whereby:

(1) Applicable Protective Requirements for Different Forms of the PMN Substance. The Company shall determine and implement the minimum dermal and respiratory personal protective equipment requirements for the different forms of the PMN substance according to the following table:

Physical Forms	**Maximum concentration of the PMN substance**	**Minimum Dermal Protection**	**Minimum Respiratory Protection**
Powdered	Any	Full general and specific dermal protection required in a(2) and a(3).	Respiratory protection required in a(5)
Liquid polymer form	Less than or equal to 7%	Full general and specific dermal protection required in a(2) and a(3).	None required provided there is no generation of vapor, mist, or aerosol and the concentration of the PMN substance is less than or equal to 7%, otherwise respiratory protection required in a(5)
Solid polymer form	Less than or equal to 30%	If there is no generation of dust and the concentration of the PMN substance is less than or equal to 30%, none required. Otherwise, full general and specific dermal protection required in a (2) and a (3).	If there is no generation of dust and the concentration of the PMN substance is less than or equal to 30%, none required. . Otherwise, respiratory protection required in a(5).

(2) General Dermal Protection. When required by the table in subparagraph a(1) of this section, each person who is reasonably likely to be dermally exposed in the work area to the PMN substance through direct handling of the substance or through contact with equipment on which the substance may exist, is required to wear, at a minimum, personal protective equipment that provides a barrier to prevent dermal exposure to the substance as specified in the minimum dermal protection column of the table in subparagraph (a)(1) in the specific work area where the substance are selected for use. Each such item of personal protective equipment must be selected and used in accordance with OSHA dermal protection requirements at 29 CFR 1910.132, 1910.133, and 1910.138.

(3) Specific Dermal Protective Equipment. When required by the table in subparagraph (a)(1) of this section, the dermal personal protective equipment required by subparagraph (a)(2) must include, but is not limited to, the following items:

(i) Gloves impervious to the PMN substance.

(ii) Full body clothing impervious to the PMN substance.

(4) Demonstration of Imperviousness. The Company must be able to demonstrate that each item of chemical protective clothing selected, including gloves, provides an impervious barrier to prevent dermal exposure during normal and expected duration and conditions of exposure within the work area by any one or a combination of the following:

(i) Testing. Testing the material used to make the chemical protective clothing and the construction of the clothing to establish that the protective clothing will be impervious for the expected duration and conditions of exposure. The testing must subject the chemical protective clothing to the expected conditions of exposure, including the likely combinations of chemical substance to which the clothing may be exposed in the work area. Testing may be conducted

according to the American Society for Testing and Materials ("ASTM") F739 "Standard Test Method for Resistance of Protective Clothing materials to Permeation by Liquids or Gases." Results shall be recorded as a cumulative permeation rate as a function of time, and shall be documented in accordance with ASTM F739 using the format specified in ASTM F1194-89 "Guide for Documenting the Results of Chemical Permeation Testing on Protective Clothing Materials." Testing may also be conducted according to the ASTM F1671-07 "Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-Borne Pathogens Using Phi-X174 Bacteriophage Penetration as a Test System". Gloves may not be used for a time period longer than they are actually tested and must be replaced at the end of each work shift during which they are exposed to the PMN substance.

(ii) Manufacturer's Specifications. Evaluating the specifications from the manufacturer or supplier of the chemical protective clothing, or of the material used in construction of the clothing, to establish that the chemical protective clothing will be impervious to the PMN substance alone and in likely combination with other chemical substance in the work area.

(5) Respiratory Protection. When required by the table in subparagraph (a)(1) of this section, each person who is reasonably likely to be exposed by inhalation in the work area to the PMN substance, is provided with, and is required to wear, at a minimum, a NIOSH-certified respirator from the respirators listed in subparagraph (a)(6) of this section, and the respirator is used in accordance with the Occupational Safety and Health Administration ("OSHA") and NIOSH respiratory protection requirements at 29 CFR 1910.134 and 42 CFR Part 84. All respirators must be issued, used, and maintained according to an appropriate respiratory protection program under the OSHA requirements in 29 CFR 1910.134.

(6) Authorized Respirators. The following NIOSH-certified respirators meet the minimum requirements for subparagraph (a)(5) of this section: NIOSH-certified air-purifying, tight-fitting full-face respirator equipped with N-100, P-100, or R-100 filter; a NIOSH-certified powered air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of an APF of 1,000; a NIOSH-certified continuous flow supplied air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of an APF of 1,000; or a NIOSH-certified continuous flow supplied air-purifying respirator with a loose-fitting hood or helmet and a HEPA filter with documented evidence of an APF of 1,000.

MANUFACTURING

(a)(1) Prohibition. The Company shall not cause, encourage, or suggest the manufacture or import of the PMN substance by any other person.

(2) Sunset Following SNUR. Subparagraph (a)(1) of this Section shall expire 75 days after promulgation of a final significant new use rule ("SNUR") governing the PMN substance under section 5(a)(2) of TSCA unless the Company is notified on or before that day of an action in a Federal Court seeking judicial review of the SNUR. If the Company is so notified, subparagraph (a)(1) shall not expire until EPA notifies the Company in writing that all Federal Court actions involving the SNUR have been resolved and the validity of the SNUR affirmed.

(3) Notice of SNUR. When EPA promulgates a final SNUR for the PMN substance and subparagraph (a)(1) of this Section expires in accordance with subparagraph (a)(2) of this Section, the Company shall notify each person whom it causes, encourages or suggests to manufacture or import the PMN substance of the existence of the SNUR.

(b) Import Only. The Company shall not manufacture the PMN substance in the United States.

(c) Prohibited Uses. The Company shall not:

(1) manufacture or import the PMN substance for use other than as: [redacted];

(2) manufacture or import the non-exempt PMN substance for commercial or consumer use, or in a consumer product.

(d) Sample. The Company shall provide to EPA a 1 gram sample of the PMN substance as specified by EPA in a future written request along with a copy of the MSDS for the substance.

PROCESSING AND USE

(a) The Company shall not process or use the PMN substance other than as: [redacted]; and

(b) The Company shall not process or use the non-exempt PMN substance for commercial or consumer use, or in a consumer product.

DISTRIBUTION

(a) Export Notice Requirement. No later than the date of distribution, the Company shall notify in writing any person to whom it distributes the PMN substances (a Distributee) that, due to the issuance of this Modified Consent Order under section 5(e) of TSCA, the PMN substances are subject to the export notification requirements of TSCA section 12(b) and 40 CFR Part 707 Subpart D. Such notice shall contain, in the form in which they appear in the Modified Consent Order, the following information: (1) the PMN or accession numbers and (2) either (A) the specific chemical identities of the chemical substances, or (B) if the specific chemical identities are confidential, the generic chemical identities.

(b) Types of Distributees. This Distribution section authorizes the Company to distribute the PMN substances to three types of Distributees: (1) Distributees who will further distribute the PMN substances only when the PMN substances are in a exempted or mitigated state, as defined in paragraph (c); (2) Distributees who will further distribute the PMN substances in a non-exempted and unmitigated state after the attached Consent Order for Processor expires 75 days after promulgation of a final SNUR governing all of the PMN substance; and (3) Distributees who will further distribute the PMN substances in a non-exempted and unmitigated state before the attached Consent Order for Processor expires 75 days after promulgation of a final SNUR governing all of the PMN substances . The distribution requirements for the first two types of Distributees are identical and are stated in paragraph (e) below. The third type of Distributee must sign the attached Consent Order for Processor, as specified in paragraph (f) below.

(c) Mitigated and Exempted States of the PMN Substance.

(1) Exempted State of the PMN Substance. As described in paragraph (b) of the Scope of Applicability and Exemptions Section, several exempted states of the PMN substance for purposes of further distribution are:

(i) completely reacted (cured);

(ii) incorporated or embedded into a polymer matrix that itself has been reacted (cured); or

(iii) incorporated or embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30% that is not intended to undergo further processing, except for mechanical processing.

(2) Mitigated States of the PMN Substance. Additionally, for purposes of further distribution, the PMN substance shall be considered to be in a "mitigated state" (regarding risk) when the PMN substances are:

(i) incorporated or embedded in a solid polymer form with a concentration of the PMN substance equal to or below 30%

(d) Temporary Transport and Storage. Notwithstanding paragraphs (e) and (f) in this Distribution section, the Company may distribute the PMN substances outside the Company for temporary transport and storage in sealed containers provided the following two conditions are met:

(1) Subsequent to any such exempt temporary transport or storage of sealed containers, the PMN substances may be distributed only to the Company or to a Distributee compliant with paragraph (e) or (f).

(2) Any human exposure or environmental release resulting from opening the sealed containers and removing or washing out the PMN substances may occur only while the PMN

substances are in the possession and control of the Company or a Distributee compliant with paragraph (e) or (f).

(e) Distribution Requirements in the Absence of Processor Order. Except when the PMN substances are in a exempted or mitigated state as described in paragraph (c) above, or as provided in the Temporary Transport and Storage paragraph (d) above, or for Distributees who sign Processor Orders as described in paragraph (f) below, the Company shall distribute the PMN substance outside the Company, other than for disposal, only to a Distributee who has agreed in writing prior to the date of distribution, to:

(1) Notify in writing any person to whom it distributes the PMN substance that, due to the issuance of this Modified Consent Order under section 5(e) of TSCA, the PMN substance is subject to the export notification requirements of TSCA section 12(b) and 40 CFR Part 707 Subpart D. Such notice shall contain, in the form in which it appears in this Modified Consent Order, the following information: (1) the PMN or accession number, and (2) either (A) the specific chemical identity of the PMN substance, or (B) if the specific chemical identity is confidential, the generic chemical identity.

(2) Not further distribute the PMN substance, to any other person, other than for disposal, until after the PMN substance is in an exempted or mitigated state as described in subparagraph (c) of this Section. Thus, further distribution for processing and use may occur once the PMN substance is in an exempted or mitigated state. However, the mitigated states are not exempted and the person receiving the PMN substance must agree in writing prior to the date of distribution to subparagraphs (e)(1)-(6) of this Distribution Section.

(3) Comply with the same requirements and restrictions required of the Company in the

Protection in the Workplace section.

(4) Not process or use the non-exempt PMN substance other than as: [redacted].

(5) Not use the non-exempt PMN substance for commercial or consumer use, or in a consumer product.

(6) Comply with the same environmental release restrictions required of the Company in the Release to Water Section of the Order.

(f) Consent Order for Processor.

(1) If the Company distributes the PMN substances to Distributees who will further distribute the PMN substances in an a non-exempted and unmitigated state, before the attached Modified Consent Order for Processor expires 75 days after promulgation of a final SNUR governing all of the PMN substances, the Company shall distribute the PMN substances outside the Company, other than for disposal, only to a Distributee who has signed the Consent Order for Processor in Attachment C to this Order (a "Processor").

(2) The Company shall obtain from each such Processor a signed copy of the Consent Order for Processor and submit the copy to EPA along with the name, address, and telephone number of a responsible official of the Processor. The Processor or Company must receive a fully executed copy of the Consent Order for Processor from EPA before the Processor may begin to process any of the PMN substances.

(g) Sunset following SNUR.

(1) If the Company distributes the PMN substances to Distributees who will further distribute the PMN substances in a non-exempted and an unmitigated state, before the attached Consent Order for Processor expires 75 days after promulgation of a final SNUR governing all of the PMN substances, the Company shall distribute the PMN substances, other than for disposal, only to processors who have signed the attached Consent Order for Processor in accordance with paragraph (f) of this Distribution section. After the attached Consent Order for Processor expires 75 days after promulgation of a final SNUR governing all of the PMN substances, the Company shall distribute the PMN substances only to Distributees who comply with the requirements specified in paragraph (e) of this Distribution section.

(2) Paragraphs (e) and (f) of this Distribution section shall expire 75 days after promulgation of a final SNUR for the PMN substances under section 5(a)(2) of TSCA, unless the Company is notified on or before that day of an action in a Federal Court seeking judicial review of the SNUR. If the Company is so notified, paragraphs (e)(2) and (f) of this Distribution section shall not expire until EPA notifies the Company in writing that all Federal Court actions involving the SNUR have been resolved and the validity of the SNUR affirmed.

(3) When EPA promulgates a final SNUR for the PMN substances and paragraph (e) of this Distribution section expires in accordance with subparagraph (g)(2), the Company shall notify each Distributee to whom it distributes the PMN substances of the existence of the SNUR. Such notification must be in writing and must specifically include all limitations contained in the SNUR which are defined as significant new uses, and which would invoke significant new use notification to EPA for the PMN substances. Such notice must also reference the publication of

the SNUR for these PMN substances in either the Federal Register or the Code of Federal Regulations. After promulgation of a SNUR and expiration of paragraphs (e)(2) and (f), such notice may substitute for the written agreement required in the introductory clause of paragraph (f); so that, if the Company provides such notice to the Distributee, then the Company is not required to obtain from such Distributee the written agreement specified in paragraph (e). However, even absent such written agreement, the Company remains obligated to comply with the "Recipient Non-Compliance" paragraph (h) below.

(h) Recipient Non-Compliance. If, at any time after commencing distribution in commerce of the PMN substances, the Company obtains knowledge that a recipient (including a Processor) of the PMN substances has failed to comply with any of the applicable conditions specified in paragraphs (e) or (f) of this Distribution section or, after paragraphs (e) or (f) expires in accordance with paragraph (g)(2), has engaged in a significant new use of the PMN substances (as defined in 40 CFR Part 721, Subpart E) without submitting a significant new use notice to EPA, the Company shall cease supplying the substances to that recipient, unless the Company is able to document each of the following:

(1) That the Company has, within 5 working days, notified the recipient in writing that the recipient has failed to comply with any of the applicable conditions specified in paragraphs (e) or (f) of this Distribution section, or has engaged in a significant new use of the PMN substances without submitting a significant new use notice to EPA.

(2) That, within 15 working days of notifying the recipient of the noncompliance, the Company received from the recipient, in writing, a statement of assurance that the recipient is aware of the applicable terms of paragraphs (e) or (f) of this Distribution section and will comply

with those terms, or is aware of the terms of the significant new use rule for the PMN substances and will not engage in a significant new use without submitting a significant new use notice to EPA.

(3) If, after receiving a statement of assurance from a recipient under subparagraph (h)(2) of this Distribution section, the Company obtains knowledge that the recipient has failed to comply with any of the applicable conditions specified in paragraphs (e) or (f) of this Distribution section, or has engaged in a significant new use of the PMN substances without submitting a significant new use notice to EPA, the Company shall cease supplying the PMN substances to that recipient, shall notify EPA of the failure to comply, and shall resume supplying the PMN substances to that recipient only upon written notification from the Agency.

RELEASE TO WATER

This provision does not supersede or preempt any applicable federal, state, and local laws and regulations. (Those other laws may be more stringent than the requirements below.) The Company is prohibited from any predictable or purposeful release of the PMN substance, or any waste stream from processing and use containing the PMN substance into the waters of the United States. This prohibition does not apply to quantities of the PMN substance embedded in solid polymer form with a concentration of the PMN substance equal to or below 30%.

RECORDKEEPING

(a) Records. After the effective date of this Order and, consistent with any other requirements

under TSCA, the Company shall maintain the following records until 5 years after the date they are created and shall make them available for inspection and copying by EPA in accordance with section 11 of TSCA:

(1) Exemptions. Records documenting that the PMN substance did in fact qualify for any one or more of the exemptions described in Section I, Paragraph (b) of this Order. Such records must satisfy all the statutory and regulatory recordkeeping requirements applicable to the exemption being claimed by the Company. Any amounts or batches of the PMN substance eligible for the Export exemption in Section I, Paragraph (b)(2) of this Order, are exempt from all the requirements in this Recordkeeping section, if the Company maintains, for 5 years from the date of their creation, copies of the export label and export notice to EPA, required by TSCA sections 12(a)(1)(B) and 12(b), respectively. Any amounts or batches of the PMN substance eligible for the Research and Development exemption in Section I, Paragraph (b)(3) of this Order, are exempt from all the requirements in this Recordkeeping section, if the Company maintains, for 5 years from the date of their creation, the records required by 40 CFR 720.78(b). For any amounts or batches of the PMN substance claimed to be eligible for any other exemption described in Section I, Paragraph (b) of this Order, the Company shall keep records demonstrating qualification for that exemption as well as the records specified in paragraphs (2) and (3) below, but is exempt from the other recordkeeping requirements in this Recordkeeping section;

(2) Records documenting the manufacture and importation volume of the PMN substance and the corresponding dates of manufacture and import;

(3) Records documenting the names and addresses (including shipment destination address, if different) of all persons outside the site of manufacture or import to whom the Company directly sells or transfers the PMN substance, the date of each sale or transfer, and the

quantity of the substance sold or transferred on such date;

(4) Records documenting the addresses of all sites of manufacture, import, processing, and use;

(5) Records documenting establishment and implementation of a program for the use of any applicable personal protective equipment required pursuant to the Protection in the Workplace section of this Order;

(6) Records documenting the determinations required by the Protection in the Workplace section of this Order that chemical protective clothing is impervious to the PMN substance;

(7) Records documenting compliance with any applicable manufacturing, processing, use, and distribution restrictions in the Manufacturing, Processing, and Use, and Distribution sections of this Order, including distributees' written agreement to comply with the Distribution section of this Order;

(8) Copies of any Transfer Documents and notices required by the Successor Liability section of this Order, if applicable; and

(9) The Company shall keep a copy of this Order at each of its sites where the PMN substance are manufactured of imported.

(b) Applicability. The provisions of this Recordkeeping Section are applicable only to activities of the Company and its Contract Manufacturer, if applicable, and not to activities of the Company's customers.

(c) OMB Control Number. Under the Paperwork Reduction Act and its regulations at 5 CFR Part 1320, particularly 5 CFR 1320.5(b), the Company is not required to respond to this "collection of

information" unless this Order displays a currently valid control number from the Office of Management and Budget ("OMB"), and EPA so informs the Company. The "collection of information" required in this TSCA §5(e) Modified Consent Orders has been approved under currently valid **OMB Control Number 2070-0012.**

IV. REQUESTS FOR PRE-INSPECTION INFORMATION

(a) EPA's Request for Information. Pursuant to section 11 of TSCA and 40 CFR 720.122, EPA may occasionally conduct on-site compliance inspections of Company facilities and conveyances associated with the PMN substance. To facilitate such inspections, EPA personnel may contact the Company in advance to request information pertinent to the scheduling and conduct of such inspections. Such requests may be written or oral. The types of information that EPA may request may include, but are not limited to, the following:

(i) Expected dates and times when the PMN substance will be in production within the subsequent 12 months;

(ii) Current workshift schedules for workers who are involved in activities associated with the PMN substance and may reasonably be exposed to the PMN substance;

(iii) Current job titles or categories for workers who are involved in activities associated with the PMN substance and may reasonably be exposed to the PMN substance;

(iv) Existing exposure monitoring data for workers who are involved in activities associated with the PMN substance and may reasonably be exposed to the PMN substance;

(v) Records required by the Recordkeeping section of this Order; and/or

(vi) Any other information reasonably related to determining compliance with this Order or conducting an inspection for that purpose.

(b) Company's Response. The Company shall respond to such requests within a reasonable period of time, but in no event later than 30 days after receiving EPA's request. When requested in writing by EPA, the Company's response shall be in writing. To the extent the information is known to or reasonably ascertainable to the Company at the time of the request, the Company's response shall demonstrate a good faith effort to provide reasonably accurate and detailed answers to all of EPA's requests.

(c) Confidential Business Information. Any Confidential Business Information ("CBI") that the Company submits to EPA pursuant to paragraph (b) shall be protected in accordance with §14 of TSCA and 40 CFR Part 2.

V. SUCCESSOR LIABILITY UPON TRANSFER OF MODIFIED CONSENT ORDER

(a) Scope. This section sets forth the procedures by which the Company's rights and obligations under this Order may be transferred when the Company transfers its interests in the PMN substance, including the right to manufacture the PMN substance, to another person outside the Company (the "Successor in Interest").

(b) Relation of Transfer Date to Notice of Commencement ("NOC").

(1) Before NOC. If the transfer from the Company to the Successor in Interest is effective before EPA receives a notice of commencement of manufacture or import ("NOC") for the PMN substance from the Company pursuant to 40 CFR 720.102, the Successor in Interest must submit new PMNs to EPA and comply fully with Section 5(a)(1) of TSCA and 40 CFR part 720 before

commencing manufacture or import of the PMN substance.

(2) After NOC. If the transfer from the Company to the Successor in Interest is effective after EPA receives a NOC, the Successor in Interest shall comply with the terms of this Order and shall not be required to submit new PMNs to EPA.

(c) Definitions. The following definitions apply to this Successor Liability section of the Order:

(1) "Successor in Interest" means a person outside the Company who has acquired the Company's full interest in the rights to manufacture the PMN substance, including all ownership rights and legal liabilities, through a transfer document signed by the Company, as transferor, and the Successor in Interest, as transferee. The term excludes persons who acquire less than the full interest of the Company in the PMN substance, such as a licensee who has acquired a limited license to the patent or manufacturing rights associated with the PMN substance. A Successor in Interest must be incorporated, licensed, or doing business in the United States in accordance with 40 CFR 720.22(a)(3).

(2) "Transfer Document" means the legal instrument(s) used to convey the interests in the PMN substance, including the right to manufacture the PMN substance, from the Company to the Successor in Interest.

(d) Notices.

(1) Notice to Successor in Interest. On or before the effective date of the transfer, the Company shall provide to the Successor in Interest, by registered mail, a copy of the Modified Consent Order and the "Notice of Transfer" document which is incorporated by reference as Attachment C to this Order.

(2) Notice to EPA. Within 10 business days of the effective date of the transfer, the Company shall, by registered mail, submit the fully executed Notice of Transfer document to: U.S. Environmental Protection Agency, New Chemicals Branch (7405), 1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460.

(3) Transfer Document. Copies of the Transfer Document must be maintained by the Successor in Interest at its principal place of business, and at all sites where the PMN substance are manufactured or imported. Copies of the Transfer Document must also be made available for inspection pursuant to Section 11 of TSCA, must state the effective date of transfer, and must contain provisions which expressly transfer liability for the PMN substance under the terms of this Order from the Company to the Successor in Interest.

(e) Liability.

(1) The Company shall be liable for compliance with the requirements of this Order until the effective date of the transfer described above.

(2) The Successor in Interest shall be liable for compliance with the requirements of this Order effective as of the date of transfer.

(3) Nothing in this section shall be construed to prohibit the Agency from taking enforcement action against the Company after the effective date of the transfer for actions taken, or omissions made, during the time in which the Company manufactured, processed, used, distributed in commerce, or disposed of the PMN substance pursuant to the terms of this Modified Consent Order.

(f) Obligations to Submit Test Data under Modified Consent Order. If paragraph (d) of the

Testing section of this Modified Consent Order requires the Company to submit test data to EPA at a specified production volume ("test trigger"), the aggregate volume of the PMN substance manufactured and imported by the Company up to the date of transfer shall count towards the test trigger applicable to the Successor in Interest.

VI. MODIFICATION AND REVOCATION OF MODIFIED CONSENT ORDER

The Company may petition EPA at any time, based upon new information on the health effects of, or human exposure to, the PMN substance, to modify or revoke substantive provisions of this Order. The exposures and risks identified by EPA during its review of the PMN substance and the information EPA determined to be necessary to evaluate those exposures and risks are described in the preamble to this Order. However, in determining whether to amend or revoke this Order, EPA will consider all relevant information available at the time the Agency makes that determination, including, where appropriate, any reassessment of the test data or other information that supports the findings in this Order, an examination of new test data or other information or analysis, and any other relevant information.

EPA will issue a modification or revocation if EPA determines that the activities proposed therein will not present an unreasonable risk of injury to health or the environment and will not result in significant or substantial human exposure or substantial environmental release in the absence of data sufficient to permit a reasoned evaluation of the health or environmental effects of the PMN substance.

In addition, the Company may petition EPA at any time to make other modifications to the language of this Order. EPA will issue such a modification if EPA determines that the modification is useful, appropriate, and consistent with the structure and intent of this Order as issued.

VII. EFFECT OF MODIFIED CONSENT ORDER

(a) Waiver. By consenting to the entry of this Order, the Company waives its rights to file objections to this Order pursuant to section 5(e)(1)(C) of TSCA, to receive service of this Order no later than 45 days before the end of the review period pursuant to section 5(e)(1)(B) of TSCA, and to challenge the validity of this Order in any subsequent action. Consenting to the entry of this Order, and agreeing to be bound by its terms, do not constitute an admission by the Company as to the facts or conclusions underlying the Agency's determinations in this proceeding. This waiver does not affect any other rights that the Company may have under TSCA.

(b) CBI Brackets. By signing this Order, the Company represents that it has carefully reviewed this document and hereby agrees that all information herein that is claimed as confidential by the Company (per section 14 of TSCA, 40 CFR Part 720 Subpart E, and 40 CFR Part 2) is correctly identified within brackets and that any information that is not bracketed is not claimed as confidential. To make this document available for public viewing, EPA will remove only the information contained within the brackets.

12/1/10
Date

Jim Willis, Director
Chemical Control Division
Office of Pollution Prevention and Toxics

12/14/2010
Date

[redacted]
Name: [redacted]
Title: [redacted]
Company: [redacted]

ATTACHMENT A

DEFINITIONS

[Note: The attached Order may not contain some of the terms defined below.]

"Chemical name" means the scientific designation of a chemical substance in accordance with the nomenclature system developed by the International Union of Pure and Applied Chemistry or the Chemical Abstracts Service's rules of nomenclature, or a name which will clearly identify a chemical substance for the purpose of conducting a hazard evaluation.

"Chemical protective clothing" means items of clothing that provide a protective barrier to prevent dermal contact with chemical substance of concern. Examples can include, but are not limited to: full body protective clothing, boots, coveralls, gloves, jackets, and pants.

"Company" means the person or persons subject to this Order.

"Commercial use" means the use of a chemical substance or any mixture containing the chemical substance in a commercial enterprise providing saleable goods or a service to consumers (e.g., a commercial dry cleaning establishment or painting contractor).

"Common name" means any designation or identification such as code name, code number, trade name, brand name, or generic chemical name used to identify a chemical substance other than by its chemical name.

"Consumer" means a private individual who uses a chemical substance or any product containing the chemical substance in or around a permanent or temporary household or residence, during recreation, or for any personal use or enjoyment.

"Consumer product" means a chemical substance that is directly, or as part of a mixture, sold or made available to consumers for their use in or around a permanent or temporary household or residence, in or around a school, or in recreation.

"Container" means any bag, barrel, bottle, box, can, cylinder, drum, reaction vessel, storage tank, or the like that contains a hazardous chemical. For purposes of this section, pipes or piping systems, and engines, fuel tanks, or other operating systems in a vehicle, are not considered to be containers.

"Contract Manufacturer" means a person, outside the Company, who is authorized to manufacture and import the PMN substance under the conditions specified in Part II. of this Modified Consent Order and in the Consent Order for Contract Manufacturer.

"Identity" means any chemical or common name used to identify a chemical substance or a mixture containing that substance.

"Immediate use." A chemical substance is for the "immediate use" of a person if it is under

the control of, and used only by, the person who transferred it from a labeled container and will only be used by that person within the work shift in which it is transferred from the labeled container.

"Impervious." Chemical protective clothing is "impervious" to a chemical substance if the substance causes no chemical or mechanical degradation, permeation, or penetration of the chemical protective clothing under the conditions of, and the duration of, exposure.

"Manufacturing stream" means all reasonably anticipated transfer, flow, or disposal of a chemical substance, regardless of physical state or concentration, through all intended operations of manufacture, including the cleaning of equipment.

"MSDS" means material safety data sheet, the written listing of data for the chemical substance.

"NIOSH" means the National Institute for Occupational Safety and Health of the U.S. Department of Health and Human Services.

"Non-enclosed process" means any equipment system (such as an open-top reactor, storage tank, or mixing vessel) in which a chemical substance is manufactured, processed, or otherwise used where significant direct contact of the bulk chemical substance and the workplace air may occur.

"Non-industrial use" means use other than at a facility where chemical substances or mixtures are manufactured, imported, or processed.

"PMN substance" means the chemical substance described in the Premanufacture notice submitted by the Company relevant to this Order.

"Personal protective equipment" means any chemical protective clothing or device placed on the body to prevent contact with, and exposure to, an identified chemical substance or substance in the work area. Examples include, but are not limited to, chemical protective clothing, aprons, hoods, chemical goggles, face splash shields, or equivalent eye protection, and various types of respirators. Barrier creams are not included in this definition.

"Process stream" means all reasonably anticipated transfer, flow, or disposal of a chemical substance, regardless of physical state or concentration, through all intended operations of processing, including the cleaning of equipment.

"Scientifically invalid" means any significant departure from the EPA-approved protocol or the Good Laboratory Practice Standards at 40 CFR Part 792 without prior or subsequent Agency approval that prevents a reasoned evaluation of the health or environmental effects of the PMN substance.

"Scientifically equivocal data" means data which, although developed in apparent

conformity with the Good Laboratory Practice Standards and EPA-approved protocols, are inconclusive, internally inconsistent, or otherwise insufficient to permit a reasoned evaluation of the potential risk of injury to human health or the environment of the PMN substance.

"Sealed container" means a closed container that is physically and chemically suitable for long-term containment of the PMN substance, and from which there will be no human exposure to, nor environmental release of, the PMN substance during transport and storage.

"Use stream" means all reasonably anticipated transfer, flow, or disposal of a chemical substance, regardless of physical state or concentration, through all intended operations of industrial, commercial, or consumer use.

"Waters of the United States" has the meaning set forth in 40 CFR 122.2.

"Work area" means a room or defined space in a workplace where the PMN substance is manufactured, processed, or used and where employees are present.

"Workplace" means an establishment at one geographic location containing one or more work areas.

ATTACHMENT B

NOTICE OF TRANSFER OF TOXIC SUBSTANCE CONTROL ACT SECTION 5(e) MODIFIED CONSENT ORDER

_____ _____

Company (Transferor) PMN Number

1. Transfer of Manufacture Rights. Effective on _____, the Company did sell or otherwise transfer to _____, ("Successor in Interest") the rights and liabilities associated with manufacture of the above-referenced chemical substance, which was the subject of a premanufacture notice ("PMN") and is governed by a Consent Order issued by the U.S. Environmental Protection Agency ("EPA") under the authority of §5(e) of the Toxic Substance Control Act (TSCA, 15 U.S.C. §2604(e)).

2. Assumption of Liability. The Successor in Interest hereby certifies that, as of the effective date of transfer, all actions or omissions governed by the applicable Consent Order limiting manufacture, processing, use, distribution in commerce and disposal of the PMN substance, shall be the responsibility of the Successor in Interest. Successor in Interest also certifies that it is incorporated, licensed, or doing business in the United States in accordance with 40 CFR 720.22(a)(3).

3. Confidential Business Information. The Successor in Interest hereby:

___ reasserts,
___ relinquishes, or
___ modifies

all Confidential Business Information ("CBI") claims made by the Company, pursuant to Section 14 of TSCA and 40 CFR part 2, for the PMN substance(s). Where "reasserts" or "relinquishes" is indicated, that designation shall be deemed to apply to all such claims. Where "modifies" is indicated, such modification shall be explained in detail in an attachment to this Notice of Transfer. Information which has been previously disclosed to the public (e.g., a chemical identity that was not claimed as CBI by the original submitter) would not subsequently be eligible for confidential treatment under this Notice of Transfer.

TOXIC SUBSTANCE CONTROL ACT
SECTION 5(e) MODIFIED CONSENT ORDER

NOTICE OF TRANSFER
(continued)

Company (Transferor)	PMN Number
Signature of Authorized Official	Date
Printed Name of Authorized Official	
Title of Authorized Official	
Successor in Interest	
Signature of Authorized Official	Date
Printed Name of Authorized Official	
Title of Authorized Official	
Address	
City, State, Zip Code	

TOXIC SUBSTANCE CONTROL ACT
SECTION 5(e) MODIFIED CONSENT ORDER

NOTICE OF TRANSFER
(continued)

_____
Successor's Technical Contact

_____
Address

_____
City, State, Zip Code

_____
Phone

Focus Report

New Chemicals Program

PMN Number: **P-09-0188**

Focus Date:	02/19/2009 12:00:00 AM	Report Status:	Completed
Consolidated Set:			
Focus Chair:	Audrey Binder	Contractor:	Paul Sohi

I. Notice Information

Submitter: [redacted]

CAS Number:

Chemical Name: Multi-walled carbon nanotubes

Use: [redacted]

Other Uses: [redacted]

PV-Max:

Manufacture:

Import: X

II. SAT Results

(1) **Health Rating:** 2 **Eco Rating:** 1 **Comments:** ;

Occupational: 2C **Non-Occupational:** **Environmental:**

(1) **PBT:** 3 U 2 **Comments:**

Awaiting Human Health Entry

Awaiting Human Health Entry

Awaiting Human Health Entry

III. OTHER FACTORS

Categories:

Health Chemical Category:

Ecotox SAR and TSCA New Chemical Category: neutral organic chemicals;

Related Cases/Regulatory History:

Health related Cases:

Ecotox Related Cases: [redacted]

Regulatory History:

[redacted] - PENDING STANDARD REVIEW
- PENDING STANDARD REVIEW
- PENDING STANDARD REVIEW
- REG 5E CONS. ORDER/TEST TRIG./SNUR

MSDS/Label Information:

MSDS: Yes Label: No

General Equipment:	provide ventilation if necessary to control exposure levels belo wairborne exposure limits / if practical, use local mechanical exhaust ventilation at sources of air contamination such as process equipment/ chemical resistant clothing and gloves/ chemical goggles.
Respirator:	above exposure limits, use NIOSH approved respiratory protection
Health Effects:	may cause eye irriation/ may cause irritation of respiratory tract/ prolonged or repeated contact may dry skin and cause irritation
TLV/PEL (PMN or raw material):	- [redacted] - TWA - ACGIH - [redacted] - PEL (respirable fraction) - OSHA - [redacted] - PEL (total dust) - OSHA - [redacted] - PEL (5 mg/m3 - respirable fraction; 15 mg/m3 total dust) - OSHA - [redacted] - TWA - ACGIH - [redacted] - PEL - OSHA

Exposure Based Information:

Exposure Based Review:	N	Exposure Based Review (Health):	N
Exposure Based Review (Eco):	N	Exposure Based (Occupational):	No
Exposure Based Review (Non Occupatuional):		Exposure Based (Environmental):	

IV. Summary of SAT Assessment

Fate:

Fate Summary:

P-09-0188
FATE:
Solid
S < 0.001 mg/L at 25 EC (E)
VP < 1.0E-6 torr at 25 EC (E)
BP > 400 EC (E)
H < 1.00E-8 (E)
POTW removal (%) = U via U
Time for complete ultimate aerobic biodeg = U
Sorption to soils/sediments = U
PBT Potential: P3BU
*CEB FATE: Migration to ground water = U

Health:

Health Summary:

Expect poor absorption via all routes (analog). Concern for irritation to eye, skin, and mucous membranes (including respiratory tract) based on analogs. Concern for lung overload for a poorly soluble particulate, and for lung effects, based on submitted test data. Possible concern for immunotoxicity and oncogenicity, based on analogs.

Test Data:

Submitted with the PMN:

Rat (F) acute oral (gavage) toxicity LD50 > 2000 mg/kg;
Rat acute dermal toxicity LD50 > 2000 mg/kg;
Eye irritant in rabbits;
Slight dermal irritant in rabbits;
Not a dermal sensitizer in mice.

Submitted with 8e)-[redacted]

Five-day rat inhalation study NOAEC 0.1 mg/m3, with increased protein concentrations, enzyme activity, cytokine and chemokine concentrations, and lymphocyte counts, observed to the end of the 28-day recovery period. In the lung, increased cytokine and chemokine concentrations, organ weights, and numbers of macrophages, and granulomatous inflammation.

Submitted with 8e)-[redacted]

Pulmonary bioassay screening study in rats (intratracheal instillation): 15% mortality within 12 hours at 1.5 mg/kg, suffocation at 5 mg/kg, with transient pulmonary inflammatory response after 24 hours, and presence of multifocal granulomas.

Ecotox:

Ecotox Values:

Fish 96-h LC50:	*(P)
Daphnid 48-h LC50:	*(P)
Green algal 96-h EC50:	*(P)
Fish Chronic Value:	*(P)
Daphnid ChV:	*(P)
Algal ChV:	*(P)

Ecotox values comments: Predictions are based on SARs for neutral organic chemicals; SAR chemical class = [redacted]-multi-walled carbon nanotubes; [redacted]; solid; log Kow >> 10 (P); S = negligible; pH7; effective concentrations based on 100% active ingredients and nominal concentrations; DW hardness < 150.0 mg/L as CaCO3; and DW TOC <2.0 mg/L;

Ecotox Factors:

Assessment Factor:	10
Concern Concentration: - Acute Value	
Concern Concentration: - Chronic Value	

V. Summary of Exposures/Releases

Engineering Summary: P-09-0188

Exposures/Releases	Release	Release	Release
Scenario	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Workers			
Exposure Type			

Engineering Summary: Exposures/Releases	Release	Release	Release
Scenario	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
Workers			
Exposure Type			

V. Summary of Exposures/Releases

Engineering Summary: P-09-0188

Exposures/Releases	Release	Release	Exposure
Scenario	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

Engineering Summary: Exposures/Releases	Exposure	Exposure	Exposure
Scenario	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

V. Summary of Exposures/Releases

Engineering Summary: P-09-0188

Exposures/Releases	Exposure	Exposure	
Scenario			

VI. Focus Decision and Rationale

Regulatory Actions

Regulatory Decision: PMN Standard Review Decision Date: 02/19/2009
Type of Decision:

Rationale: P09-0188 was placed into limited standard review for uncertain health concerns for nano sized particles. Human health concerns are moderate and there is a concern for irritation to eye, skin, and mucous membranes (including respiratory tract) based on analogs. Concern for lung overload for a poorly soluble particulate, and for lung effects, based on submitted test data. Possible concern for immunotoxicity and oncogenicity, based on analogs. Ecotoxicity concerns were low, due to no effects expected at saturation. EAB only performed a qualitative report due. The Inhalation Monitoring Criteria for the Pilot Program were met for inhalation exposures from processing and use. Inhalation monitoring is requested. Ecotoxicity category is neutral organics. For the review process a TI and schedule are needed, but no team is required.

P2 Rec Comments:

Testing:

Final Recommended:

Health:
Eco:
Fate:
Other:

SAT Report

PMN Number: **P-09-0188**
SAT Date: **2/10/2009**
Print Date: **11/6/2015**

Related cases:
Health related cases: [redacted]
Ecotox related cases: [redacted]

Concern levels:

Type of Concern:	Health	Eco	Comments
Level of Concern:	2	1	

Persistence	Bioaccum	Toxicity	Comments
3	U	2	
		Awaiting Human Health Entry	
		Awaiting Human Health Entry	
		Awaiting Human Health Entry	

Exposure Based Review:
Health: No
Ecotox: No

Routes of exposure:
Health: Inhalation, dermal, drinking water
Ecotox: No releases to water
Fate: ;

Keywords:
Keywords:

Summary of Assessment:

Fate:
Fate Summary: P-09-0188
FATE:
Solid

S < 0.001 mg/L at 25 EC (E)
VP < 1.0E-6 torr at 25 EC (E)
BP > 400 EC (E)
H < 1.00E-8 (E)
POTW removal (%) = U via U
Time for complete ultimate aerobic biodeg = U
Sorption to soils/sediments = U
PBT Potential: P3BU
*CEB FATE: Migration to ground water = U

Health:

Health Summary: Expect poor absorption via all routes (analog). Concern for irritation to eye, skin, and mucous membranes (including respiratory tract) based on analogs. Concern for lung overload for a poorly soluble particulate, and for lung effects, based on submitted test data. Possible concern for immunotoxicity and oncogenicity, based on analogs.

Test Data: Submitted with the PMN:

Rat (F) acute oral (gavage) toxicity LD50 > 2000 mg/kg;
Rat acute dermal toxicity LD50 > 2000 mg/kg;
Eye irritant in rabbits;
Slight dermal irritant in rabbits;
Not a dermal sensitizer in mice.

Submitted with 8e)-[redacted]

Five-day rat inhalation study NOAEC 0.1 mg/m3, with increased protein concentrations, enzyme activity, cytokine and chemokine concentrations, and lymphocyte counts, observed to the end of the 28-day recovery period. In the lung, increased cytokine and chemokine concentrations, organ weights, and numbers of macrophages, and granulomatous inflammation.

Submitted with 8e)-[redacted]:

Pulmonary bioassay screening study in rats (intratracheal instillation): 15% mortality within 12 hours at 1.5 mg/kg, suffocation at 5 mg/kg, with transient pulmonary inflammatory response after 24 hours, and presence of multifocal granulomas.

Ecotox:

Test Organism	Test Type	Test End Point	Predicted	Measured	Comments
fish	96-h	LC50	*		
daphnid	48-h	LC50	*		
green algal	96-h	EC50	*		
fish	_	chronic value	*		

daphnid	**_**	**chronic value**	*		
algal	**_**	**chronic value**	*		
Sewage Sludge	**3-h**	**EC50**	**_**		
Sewage Sludge	**_**	**Chronic Value**	**_**		

Ecotox Values Comments: Predictions are based on SARs for neutral organic chemicals; SAR chemical class = [redacted]-multi-walled carbon nanotubes; MW>[redacted]; solid; log Kow >> 10 (P); S = negligible; pH7; effective concentrations based on 100% active ingredients and nominal concentrations; DW hardness < 150.0 mg/L as CaCO3; and DW TOC <2.0 mg/L;

Factors	Values	Comments
Assessment Factor	10	
Concentration of Concern (ppb) Acute		
Concentration of Concern (ppb) Chronic		*
SARs	neutral organic chemicals	
SAR Class	carbon allotrope	
TSCA New Chemcial Category		

Ecotox Factors Comments:

SAT Chair: J. Kwiat
Fate assessor: **Ecotox assessor:** **Health assessor:**

INITIAL REVIEW ENGINEERING REPORT [redacted]

P-09-0188
Focus Ready Draft 2/19/2009

ENGINEER: Arnold \ CPW
PV (kg/yr): [redacted]

Revision Notes/Assessment Overview:

SUBMITTER: [redacted]

USE: Component of paints, coatings, and industrial composites.

OTHER USES: [redacted]

MSDS: Yes **LABEL**: No

Gen Eqpt: provide ventilation if necessary to control exposure levels belo wairborne exposure limits/ if practical, use local mechanical exhaust ventilation at sources of air contamination such as process equipment/ chemical resistant clothing and gloves/ chemical goggles.
Respirator: above exposure limits, use NIOSH approved respiratory protection
Health Effects: may cause eye irriation/ may cause irritation of respiratory tract/ prolonged or repeated contact may dry skin and cause irritation
TLV/PEL: - [redacted] TWA - ACGIH - [redacted] - PEL (respirable fraction) - OSHA - [redacted] - PEL (total dust) - OSHA - [redacted]
LVE PPE:

CRSS: (12:00:00 AM):
Chemical Name: Multi-walled carbon nanotubes
S-H2O: g/L @
VP: 0.0E+0 torr @
MW: 0 0.0%<500 0.0%<1000
Physical State and Misc CRSS Info:
Neat: Solid **Mfg:** Solid
Proc/Form: [redacted] **End Use:** [redacted]. Submitted Data: Molecular Weight = [redacted] g/mol; Insoluble in water; Insoluble in solvents; Mean Number of Walls [redacted] Estimated Data: BP > 400 °C (High MW); VP < 0.000001 torr (High MW); WS < 0.000001 g/L (High MW).

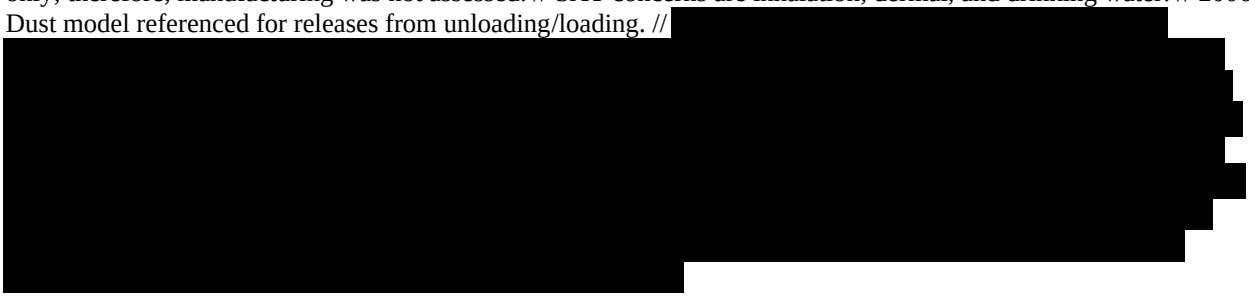
Consumer Use: No

SAT (concerns): (2/10/2009):

Related Cases and Misc SAT Info:
Migration: Unknown based on SAT
Migration to groundwater:
PBT rating: P3 **B T**2 PBT indicated as 3,U,2.
Health: 2, Dermal, Drinking Water, Inhalation
Eco: 1, No releases to Water

OCCUPATIONAL EXPOSURE RATING: 2C

NOTES & KEY ASSUMPTIONS:
Generated by the 06/07/2005 version of ChemSTEER. The following IRER is a NANO case. // The PMN is import only; therefore, manufacturing was not assessed. // SAT concerns are inhalation, dermal, and drinking water. // 2006 Dust model referenced for releases from unloading/loading. //



POLLUTION PREVENTION CONSIDERATIONS:
None.

P2 REC:

EXPOSURE-BASED REVIEW: No **(0 criteria met)**

P-09-0188

Processing - [redacted]

Number of Sites/Location: [redacted]

[redacted]

ENVIRONMENTAL RELEASES ESTIMATE SUMMARY

IRER Note: The daily releases listed for any source below may coincide with daily releases from the other sources to the same medium.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

RELEASE TOTAL

[redacted]

OCCUPATIONAL EXPOSURES ESTIMATE SUMMARY

Tot. # of workers exposed via assessed routes: [redacted]
Basis:

Dermal:

[redacted]

Inhalation:

[redacted]

INHALATION MONITORING DATA REVIEW

1) Uncertainty (estimate based on model, regulatory limit, or data not specific to industry): Yes
2) (a) Exposure level > 1 mg/day? No
(b) Hazard Rating for health of 2 or greater? Yes
Inhalation Monitoring Data Desired? Yes (both criteria met)

Dermal:

[redacted].

P-09-0188

Use - [redacted]

[redacted]

ENVIRONMENTAL RELEASES ESTIMATE SUMMARY

IRER Note: The daily releases listed for any source below may coincide with daily releases from the other sources to the same medium. Note: submission provided description or releases, but no actual release estimates. Submission indicated an unspecified release amount from filtering.

[redacted]

[redacted]

[redacted]

RELEASE TOTAL

[redacted]

OCCUPATIONAL EXPOSURES ESTIMATE SUMMARY

Tot. # of workers exposed via assessed routes: [redacted]
Basis:

Dermal:

[redacted]

[redacted]

[redacted]

INHALATION MONITORING DATA REVIEW

1) Uncertainty (estimate based on model, regulatory limit, or data not specific to industry): Yes
2) (a) Exposure level > 1 mg/day? No
(b) Hazard Rating for health of 2 or greater? Yes
Inhalation Monitoring Data Desired? Yes (both criteria met)

Dermal:

[redacted]

STANDARD REVIEW EXPOSURE REPORT

Quantitative exposure assessment for a nanomaterial based on Standard Review Engineering Report of 3/31/2009.

Chemical ID: P090188 Reviewer: Delpire

Results Table: Dose, Concentration, and Days Exceeded Results Summary

Exposure Scenario[1]	Water						Landfill	Stack Air		Fugitive Air	
Release activity(ies)[2]; exposure calculation(s)[3]	Drinking Water		Fish Ingestion		7Q10[4] CC=1	PDM Days Exceeded	LADD	ADR	LADD	ADR	LADD
	ADR	LADD	ADR	LADD							
	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	µg/l	# Days	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day
PROC: max ADR, max LADD, max acute eco, PDM	**7.22E-02**	**5.41E-04**	**0.87**	**1.16E-02**	[redacted]	**254**	**5.85E-05**	**4.80E-04**	**2.74E-05**	**4.82E-03**	**1.10E-04**
USE: max ADR, max acute eco, PDM1	**9.50E-03**	---	**0.12**	---	[redacted]	**22**	---	**1.25E-04**	---	**1.78E-03**	---
USE: PDM2	---	---	---	---	[redacted]	**145**	---	---	---	---	---
USE: max LADD	---	**2.85E-05**	---	**6.10E-04**	---	---	**8.51E-06**	---	**2.82E-06**	---	**4.54E-06**

[1] Exposure scenario titles consist of release activity followed by exposure calculation abbreviation.
[2] Release activities are from engineering report's Manufacturing (Mfg), Processing (Proc) and Use release activity labels.
Multiple release activities are combined in one exposure scenario if their releases occur at same location.
[3] Exposure calculations are Acute Dose Rate (ADR), Lifetime Average Daily Dose (LADD), and Probabilistic Dilution Model (PDM). There may be one, two, or all three exposure calculations per exposure scenario.
CC is the aquatic concentration of concern.
[4] This column displays concentration values for the 7Q10 streamflow, which is defined as the average streamflow of the 7 consecutive days of lowest flow within a 10 year period.

Remarks: This is a bounding "what if" scenario assuming 0% removal in wastewater treatment, rapid migration to groundwater, 0% destruction in incineration, BCF=5000, and COC=1ppb.

Exposure Based Criteria

Parameter	Exp Based	Persistent	Exceedance Value
Drinking (Surface) Water Dose (mg/kg/day)	N/A	**Yes**	**7.22E-02**
Fish Ingestion Dose (mg/kg/day)	N/A	**Yes**	**0.87**
Inhalation Dose (mg/kg/day)	N/A	**Yes**	**4.82E-03**
Groundwater Dose (mg/kg/day)	N/A	No	
Surface Water Release After Treatment (kg/yr)	N/A	No	
Total Release After Treatment (kg/yr)	N/A	No	

Fate test recommendations: Please see the May 15, 2009 memorandum from Jed Costanza to Kristan Markey for EAB's fate test recommendations.

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor: Delpire

ENVIRONMENTAL RELEASES

Scenario#:1 Number of Release Sites: [redacted]

Release Activity: PROC: max ADR, LADD, PDM

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 1 Number of Sites: [redacted] RELEASE ACTIVITY:PROC: max ADR, LADD, PDM

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	1.57E-05	**5.41E-04**	mg/kg/day	3.37E-04	**1.16E-02**	mg/kg/day
$LADC_{pot}$	8.05E-04	2.77E-02	mg/L	4.03	138.64	mg/kg
Acute						
ADR_{pot}	6.36E-04	**7.22E-02**	mg/kg/day	2.54E-02	**0.87**	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 1 RELEASE ACTIVITY: PROC: max ADR, LADD, PDM

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	70	**254**	[redacted]	[redacted]	[redacted]	[redacted]

Remarks: COC exceeded for > 20 days/yr

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

DRINKING WATER EXPOSURE ESTIMATES FROM LANDFILL RELEASES

SCENARIO #: 1 ACTIVITY: PROC: max ADR, LADD, PDM

RELEASE DESCRIPTION:

EXPOSED POPULATION: Adult

NUMBER OF SITES	NON-SLUDGE LANDFILL RELEASE AND DAYS OF RELEASE (kg/site/day)/(days)	LANDFILLED SLUDGE[1] AND DAYS OF RELEASE (kg/site/day)/(days)	MIGRATION DESCRIPTOR[2]	ADSORPTION TO WASTEWATER SLUDGE (%)	DRINKING WATER TREATMENT (%)
[redacted]	[redacted]	[redacted]	[redacted]	0.00	0.00

[1] Landfilled sludge equals the fraction adsorbed to wastewater treatment sludge times the surface water pre-treatment release.

[2]

Migration Descriptor	Log Koc	Groundwater Concentration (GWC) (mg/L per kg release)
Negligible	no migration	None
Negligible to slow	> 4.5	3.21E-6
Slow	<4.5 to 3.5	2.67E-5
Moderate	<3.5 to 2.5	5.95E-5
Rapid	<2.5	7.55E-5

Exposure Units	Results	ASSUMPTIONS			
		ED (years)	AT (years)	BW (kg)	IR (L/day)
Cancer					
$LADD_{pot}$ (mg/kg/day)	**5.85E-05**	30.00	75.00	71.80	1.40
$LADC_{pot}$ (mg/L)	3.00E-03	30.00	75.00	NA	NA

REMARKS:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 1 RELEASE ACTIVITY:PROC: max ADR, LADD, PDM

RELEASE DESCRIPTION:

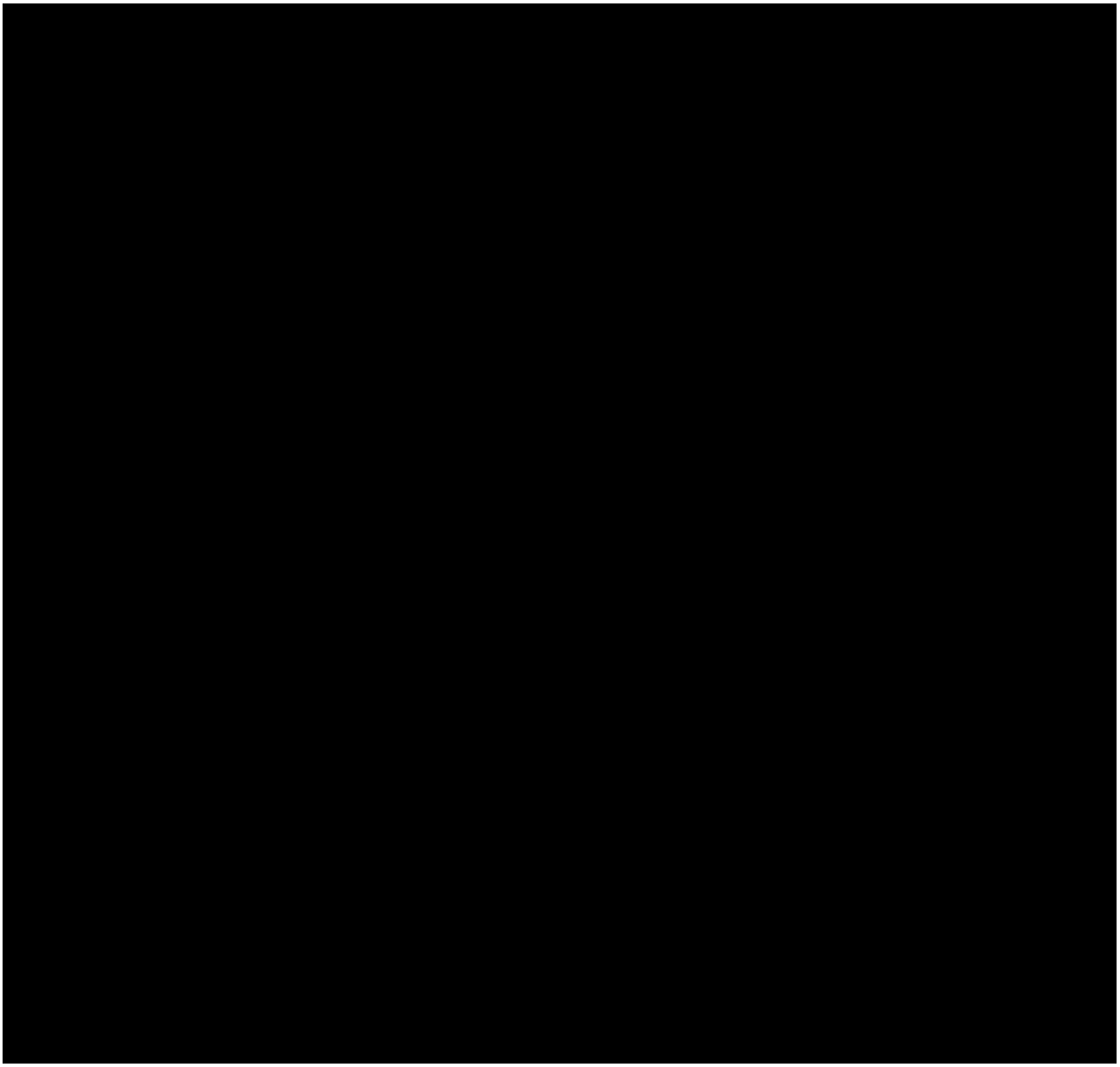
METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	[redacted]	
Per Site Fugitive Release:	[redacted]	kg/site/day
Fugitive Release Days per Year:	[redacted]	days
% Removal via Fugitive Release:	[redacted]	%
Total Fugitive Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Fugitive):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	[redacted]	µg/m^3
Per Site Stack Release:	[redacted]	kg/site/day
Stack Release Days per Year:	[redacted]	days
% Removal via Stack Release:	[redacted]	%
Total Stack Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Stack):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	[redacted]	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	**2.74E-05**	**1.10E-04**	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	1.49E-04	6.00E-04	30.00	75.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	**4.80E-04**	**4.82E-03**	NA	1 day	71.80	0.55

Inhalation Comments:



STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:2 Number of Release Sites: [redacted]

Release Activity: USE: max ADR, PDM1

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 2 Number of Sites: [redacted] RELEASE ACTIVITY:USE: max ADR, PDM1

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	2.30E-07	7.93E-06	mg/kg/day	4.94E-06	1.70E-04	mg/kg/day
$LADC_{pot}$	1.18E-05	4.07E-04	mg/L	5.91E-02	2.03	mg/kg
Acute						
ADR_{pot}	8.37E-05	**9.50E-03**	mg/kg/day	3.34E-03	**0.12**	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 2 RELEASE ACTIVITY: USE: max ADR, PDM1

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	6	**22**	[redacted]	[redacted]	0.00	High

Remarks: COC exceeded for > 20 days/yr

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 2 RELEASE ACTIVITY:USE: max ADR, PDM1

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	[redacted]	
Per Site Fugitive Release:	[redacted]	kg/site/day
Fugitive Release Days per Year:	[redacted]	days
% Removal via Fugitive Release:	[redacted]	%
Total Fugitive Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Fugitive):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	[redacted]	µg/m^3
Per Site Stack Release:	[redacted]	kg/site/day
Stack Release Days per Year:	[redacted]	days
% Removal via Stack Release:	[redacted]	%
Total Stack Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Stack):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	[redacted]	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	7.94E-07	4.54E-06	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	4.32E-06	2.47E-05	30.00	75.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	**1.25E-04**	**1.78E-03**	NA	1 day	71.80	0.55

Inhalation Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:3 Number of Release Sites: [redacted]

Release Activity: USE: PDM2

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 3 Number of Sites: [redacted] RELEASE ACTIVITY:USE: PDM2

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	6.63E-07	2.28E-05	mg/kg/day	1.42E-05	4.89E-04	mg/kg/day
$LADC_{pot}$	3.40E-05	1.17E-03	mg/L	0.17	5.85	mg/kg
Acute						
ADR_{pot}	2.51E-05	2.85E-03	mg/kg/day	1.00E-03	3.45E-02	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 3 RELEASE ACTIVITY: USE: PDM2

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	40	**145**	[redacted]	[redacted]	0.00	High

Remarks: COC exceeded for > 20 days/yr

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:4 Number of Release Sites: [redacted]

Release Activity: USE: max LADD

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES		
SCENARIO #: 4	Number of Sites: [redacted]	RELEASE ACTIVITY:USE: max LADD
SIC-CODE DESCRIPTION: [redacted]		
SIC-CODE (S): [redacted]		EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
0.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]				
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]				

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	8.27E-07	**2.85E-05**	mg/kg/day	1.77E-05	**6.10E-04**	mg/kg/day
$LADC_{pot}$	4.24E-05	1.46E-03	mg/L	0.21	7.30	mg/kg

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

DRINKING WATER EXPOSURE ESTIMATES FROM LANDFILL RELEASES

SCENARIO #: 4 ACTIVITY: USE: max LADD

RELEASE DESCRIPTION:

EXPOSED POPULATION: Adult

NUMBER OF SITES	NON-SLUDGE LANDFILL RELEASE AND DAYS OF RELEASE (kg/site/day)/(days)	LANDFILLED SLUDGE[1] AND DAYS OF RELEASE (kg/site/day)/(days)	MIGRATION DESCRIPTOR[2]	ADSORPTION TO WASTEWATER SLUDGE (%)	DRINKING WATER TREATMENT (%)
[redacted]	[redacted]	[redacted]	[redacted]	0.00	0.00

[1] Landfilled sludge equals the fraction adsorbed to wastewater treatment sludge times the surface water pre-treatment release.

[2]

Migration Descriptor	Log Koc	Groundwater Concentration (GWC) (mg/L per kg release)
Negligible	no migration	None
Negligible to slow	> 4.5	3.21E-6
Slow	<4.5 to 3.5	2.67E-5
Moderate	<3.5 to 2.5	5.95E-5
Rapid	<2.5	7.55E-5

Exposure Units	Results	ASSUMPTIONS			
		ED (years)	AT (years)	BW (kg)	IR (L/day)
Cancer					
$LADD_{pot}$ (mg/kg/day)	**8.51E-06**	30.00	75.00	71.80	1.40
$LADC_{pot}$ (mg/L)	4.37E-04	30.00	75.00	NA	NA

REMARKS:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 4 RELEASE ACTIVITY:USE: max LADD

RELEASE DESCRIPTION:

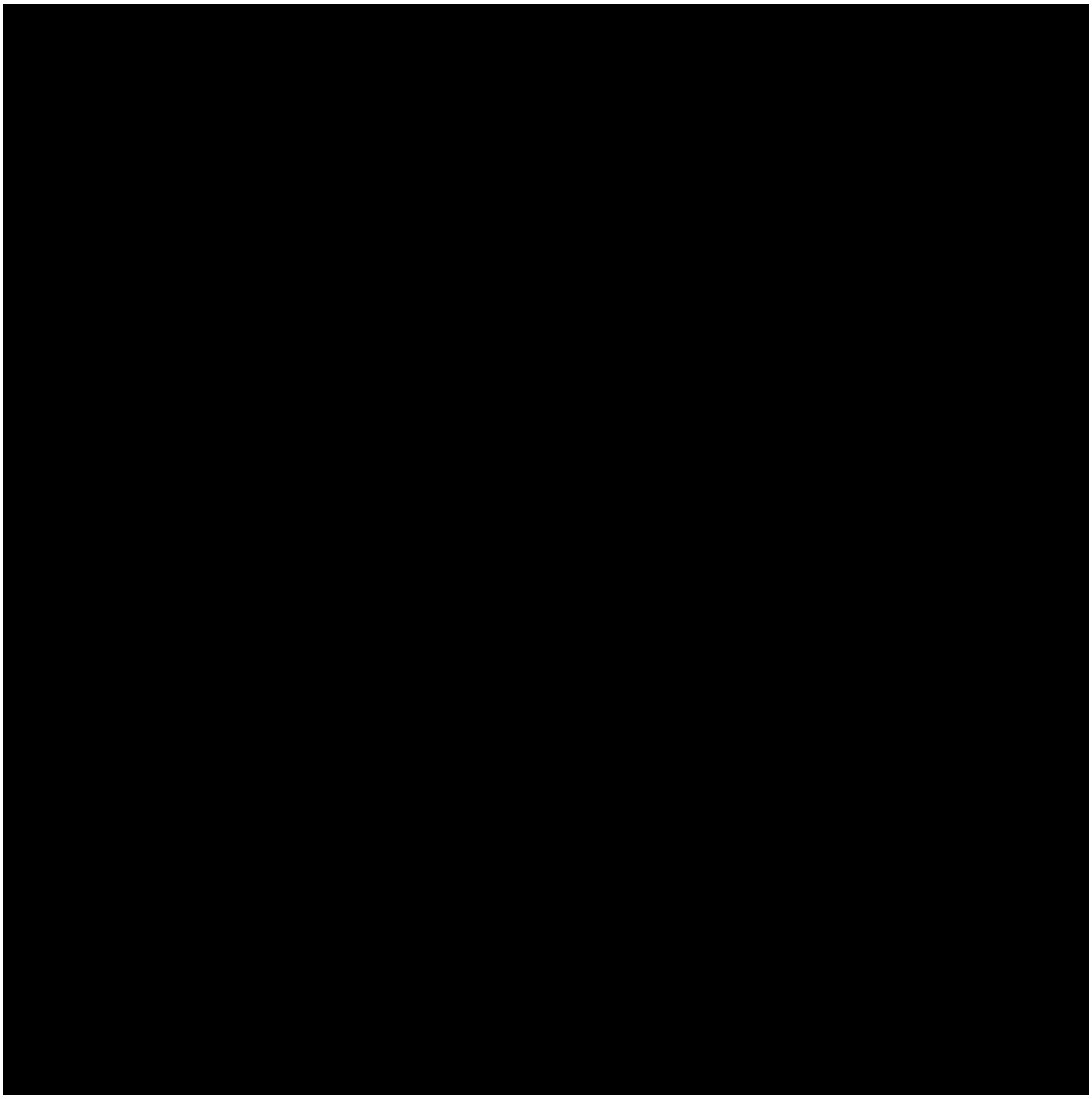
METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	[redacted]	
Per Site Fugitive Release:	[redacted]	kg/site/day
Fugitive Release Days per Year:	[redacted]	days
% Removal via Fugitive Release:	[redacted]	%
Total Fugitive Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Fugitive):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	[redacted]	µg/m^3
Per Site Stack Release:	[redacted]	kg/site/day
Stack Release Days per Year:	[redacted]	days
% Removal via Stack Release:	[redacted]	%
Total Stack Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Stack):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	[redacted]	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	**2.82E-06**	**4.54E-06**	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	1.54E-05	2.47E-05	30.00	75.00	NA	NA

Inhalation Comments:



STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Reviewer: Delpire

Results Table: Dose, Concentration, and Days Exceeded Results Summary

Exposure Scenario[1]	Water						Landfill	Stack Air		Fugitive Air	
Release activity(ies)[2]; exposure calculation(s)[3]	Drinking Water		Fish Ingestion		7Q10[4] CC=1	PDM Days Exceeded	LADD	ADR	LADD	ADR	LADD
	ADR	LADD	ADR	LADD							
	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	µg/l	# Days	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day
PROC: max ADR, max LADD, max acute eco, PDM	---	---	---	---	---	---	**1.16E-04**	**4.80E-04**	**2.74E-05**	**4.82E-03**	**1.10E-04**
USE: max ADR, max acute eco, PDM1	---	---	---	---	---	---	---	**1.25E-04**	---	**1.78E-03**	---
USE: PDM2	---	---	---	---	---	---	---	---	---	---	---
USE: max LADD	---	---	---	---	---	---	**8.51E-06**	---	**2.82E-06**	---	**4.54E-06**

[1] Exposure scenario titles consist of release activity followed by exposure calculation abbreviation.
[2] Release activities are from engineering report's Manufacturing (Mfg), Processing (Proc) and Use release activity labels.
Multiple release activities are combined in one exposure scenario if their releases occur at same location.
[3] Exposure calculations are Acute Dose Rate (ADR), Lifetime Average Daily Dose (LADD), and Probabilistic Dilution Model (PDM). There may be one, two, or all three exposure calculations per exposure scenario.
CC is the aquatic concentration of concern.
[4] This column displays concentration values for the 7Q10 streamflow, which is defined as the average streamflow of the 7 consecutive days of lowest flow within a 10 year period.

Remarks: This is a bounding "what if" scenario assuming 100% removal in wastewater treatment, 100% sorption to wastewater treatment sludge, rapid migration to groundwater, 0% destruction in incineration, BCF=5000, and COC=1ppb.

Exposure Based Criteria

Parameter	Exp Based	Persistent	Exceedance Value
Drinking (Surface) Water Dose (mg/kg/day)	N/A	No	
Fish Ingestion Dose (mg/kg/day)	N/A	No	
Inhalation Dose (mg/kg/day)	N/A	**Yes**	**4.82E-03**
Groundwater Dose (mg/kg/day)	N/A	No	
Surface Water Release After Treatment (kg/yr)	N/A	No	
Total Release After Treatment (kg/yr)	N/A	No	

Fate test recommendations: Please see the May 15, 2009 memorandum from Jed Costanza to Kristan Markey for EAB's fate test recommendations.

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor: Delpire

ENVIRONMENTAL RELEASES

Scenario#:1 Number of Release Sites: [redacted]

Release Activity: PROC: max ADR, LADD, PDM

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 1 Number of Sites: [redacted] RELEASE ACTIVITY:PROC: max ADR, LADD, PDM

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
100.00	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day
$LADC_{pot}$	N/A	N/A	mg/L	N/A	N/A	mg/kg
Acute						
ADR_{pot}	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 1 RELEASE ACTIVITY: PROC: max ADR, LADD, PDM

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	0	0	[redacted]	[redacted]	100.00	High

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

DRINKING WATER EXPOSURE ESTIMATES FROM LANDFILL RELEASES

SCENARIO #: 1 ACTIVITY: PROC: max ADR, LADD, PDM

RELEASE DESCRIPTION:

EXPOSED POPULATION: Adult

NUMBER OF SITES	NON-SLUDGE LANDFILL RELEASE AND DAYS OF RELEASE (kg/site/day)/(days)	LANDFILLED SLUDGE[1] AND DAYS OF RELEASE (kg/site/day)/(days)	MIGRATION DESCRIPTOR[2]	ADSORPTION TO WASTEWATER SLUDGE (%)	DRINKING WATER TREATMENT (%)
[redacted]	[redacted]	[redacted]	[redacted]	100.00	0.00

[1] Landfilled sludge equals the fraction adsorbed to wastewater treatment sludge times the surface water pre-treatment release.

[2]

Migration Descriptor	Log Koc	Groundwater Concentration (GWC) (mg/L per kg release)
Negligible	no migration	None
Negligible to slow	> 4.5	3.21E-6
Slow	<4.5 to 3.5	2.67E-5
Moderate	<3.5 to 2.5	5.95E-5
Rapid	<2.5	7.55E-5

Exposure Units	Results	ASSUMPTIONS			
		ED (years)	AT (years)	BW (kg)	IR (L/day)
Cancer					
$LADD_{pot}$ (mg/kg/day)	**1.16E-04**	30.00	75.00	71.80	1.40
$LADC_{pot}$ (mg/L)	5.97E-03	30.00	75.00	NA	NA

REMARKS:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 1 RELEASE ACTIVITY:PROC: max ADR, LADD, PDM

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	[redacted]	
Per Site Fugitive Release:	[redacted]	kg/site/day
Fugitive Release Days per Year:	[redacted]	days
% Removal via Fugitive Release:	[redacted]	%
Total Fugitive Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Fugitive):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	[redacted]	µg/m^3
Per Site Stack Release:	[redacted]	kg/site/day
Stack Release Days per Year:	[redacted]	days
% Removal via Stack Release:	[redacted]	%
Total Stack Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Stack):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	[redacted]	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	**2.74E-05**	**1.10E-04**	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	1.49E-04	6.00E-04	30.00	75.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	**4.80E-04**	**4.82E-03**	NA	1 day	71.80	0.55

Inhalation Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:2 Number of Release Sites: [redacted]

Release Activity: USE: max ADR, PDM1

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 2 Number of Sites: [redacted] RELEASE ACTIVITY:USE: max ADR, PDM1

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
100.00	[redacted]	[redacted]	[redacted]	0.00	5000.00

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER

PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES

Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day
$LADC_{pot}$	N/A	N/A	mg/L	N/A	N/A	mg/kg
Acute						
ADR_{pot}	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 2 RELEASE ACTIVITY: USE: max ADR, PDM1

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	0	0	[redacted]	[redacted]	100.00	High

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 2 RELEASE ACTIVITY:USE: max ADR, PDM1

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites:	[redacted]	
Per Site Fugitive Release:	[redacted]	kg/site/day
Fugitive Release Days per Year:	[redacted]	days
% Removal via Fugitive Release:	[redacted]	%
Total Fugitive Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Fugitive):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration(Fugitive):	[redacted]	µg/m^3
Per Site Stack Release:	[redacted]	kg/site/day
Stack Release Days per Year:	[redacted]	days
% Removal via Stack Release:	[redacted]	%
Total Stack Release:	[redacted]	kg/yr
Max Annual Average Air Concentration (Stack):	[redacted]	µg/m^3
Max 24 Hour Average Air Concentration (Stack):	[redacted]	µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	7.94E-07	4.54E-06	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	4.32E-06	2.47E-05	30.00	75.00	NA	NA
Acute						
ADR_{pot} (mg/kg/day)	**1.25E-04**	**1.78E-03**	NA	1 day	71.80	0.55

Inhalation Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:3 Number of Release Sites:

Release Activity: USE: PDM2

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:				
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:				
Per Site Release:				
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 3 Number of Sites: [redacted] RELEASE ACTIVITY:USE: PDM2

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
100.00	[redacted]	[redacted]	[redacted]	0.00	5000.00

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day
$LADC_{pot}$	N/A	N/A	mg/L	N/A	N/A	mg/kg
Acute						
ADR_{pot}	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC CODE EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 3 RELEASE ACTIVITY: USE: PDM2

SIC CODE DESCRIPTION: [redacted]

ASSOCIATED SIC CODES: [redacted]

SIC CODE RESULTS

COC (µg/L)	Percent of Year COC Exceeded	Number of Days COC Exceeded	Release days/year	Loading (kg/site/day)	Waste Water Treatment (%)	High/Avg Analysis
1.00	0	0	[redacted]	[redacted]	100.00	High

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188 Assessor:

ENVIRONMENTAL RELEASES

Scenario#:4 Number of Release Sites: [redacted]

Release Activity: USE: max LADD

Release Description:	WATER	LANDFILL Non-sludge/Sludge	STACK	FUGITIVE
Total Releases:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/yr)	(kg/yr)	(kg/yr)	(kg/yr)
		Non-sludge/Sludge		
Release Days/yr:	[redacted]	[redacted]	[redacted]	[redacted]
Per Site Release:	[redacted]	[redacted]	[redacted]	[redacted]
	(kg/site/day)	(kg/site/day)	(kg/site/day)	(kg/site/day)

Remarks:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

SIC-CODE BASED HUMAN AND AQUATIC EXPOSURES TO SURFACE WATER RELEASES

SCENARIO #: 4 Number of Sites: [redacted] RELEASE ACTIVITY:USE: max LADD

SIC-CODE DESCRIPTION: [redacted]

SIC-CODE (S): [redacted] EXPOSED POPULATION: Adult

WWT REMOVAL (%)	RELEASE DAYS	PRETREATMENT RELEASE (kg/site/day)	POSTTREATMENT RELEASE (kg/site/day)	DWT (%)	BCF (L/kg)
100.00	[redacted]	[redacted]	[redacted]	0.00	5000.00

AQUATIC EXPOSURE ESTIMATES - SURFACE WATER									
PLANT TYPE	% ILE FACILITY	STREAM FLOW (MLD)				STREAM CONC. (µg/l)			
		Harmonic Mean	30Q5	7Q10	1Q10	Harmonic Mean	30Q5	7Q10	1Q10
ALL	50	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
ALL	10	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

DRINKING WATER AND FISH INGESTION EXPOSURE ESTIMATES						
Exposure Units	Drinking Water Results		Drinking Water Units	Fish Ingestion Results		Fish Ingestion Units
	50%	10%		50%	10%	
Cancer						
$LADD_{pot}$	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day
$LADC_{pot}$	N/A	N/A	mg/L	N/A	N/A	mg/kg
Acute						
ADR_{pot}	N/A	N/A	mg/kg/day	N/A	N/A	mg/kg/day

SIC Code Comments:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

DRINKING WATER EXPOSURE ESTIMATES FROM LANDFILL RELEASES

SCENARIO #: 4 ACTIVITY: USE: max LADD

RELEASE DESCRIPTION:

EXPOSED POPULATION: Adult

NUMBER OF SITES	NON-SLUDGE LANDFILL RELEASE AND DAYS OF RELEASE (kg/site/day)/(days)	LANDFILLED SLUDGE[1] AND DAYS OF RELEASE (kg/site/day)/(days)	MIGRATION DESCRIPTOR[2]	ADSORPTION TO WASTEWATER SLUDGE (%)	DRINKING WATER TREATMENT (%)
[redacted]	[redacted]	[redacted]	[redacted]	100.00	0.00

[1] Landfilled sludge equals the fraction adsorbed to wastewater treatment sludge times the surface water pre-treatment release.

[2]

Migration Descriptor	Log Koc	Groundwater Concentration (GWC) (mg/L per kg release)
Negligible	no migration	None
Negligible to slow	> 4.5	3.21E-6
Slow	<4.5 to 3.5	2.67E-5
Moderate	<3.5 to 2.5	5.95E-5
Rapid	<2.5	7.55E-5

Exposure Units	Results	ASSUMPTIONS			
		ED (years)	AT (years)	BW (kg)	IR (L/day)
Cancer					
$LADD_{pot}$ (mg/kg/day)	**8.51E-06**	30.00	75.00	71.80	1.40
$LADC_{pot}$ (mg/L)	4.37E-04	30.00	75.00	NA	NA

REMARKS:

STANDARD REVIEW EXPOSURE REPORT

Chemical ID: P090188

INHALATION EXPOSURE ESTIMATES (POST-TREATMENT)

SCENARIO #: 4 RELEASE ACTIVITY:USE: max LADD

RELEASE DESCRIPTION:

METHOD OF CALCULATION: Screen3

EXPOSED POPULATION: Adult

Number of Sites: [redacted]

Per Site Fugitive Release: [redacted] kg/site/day

Fugitive Release Days per Year: [redacted] days

% Removal via Fugitive Release: [redacted] %

Total Fugitive Release: [redacted] kg/yr

Max Annual Average Air Concentration (Fugitive): [redacted] µg/m^3

Max 24 Hour Average Air Concentration(Fugitive): [redacted] µg/m^3

Per Site Stack Release: [redacted] kg/site/day

Stack Release Days per Year: [redacted] days

% Removal via Stack Release: [redacted] %

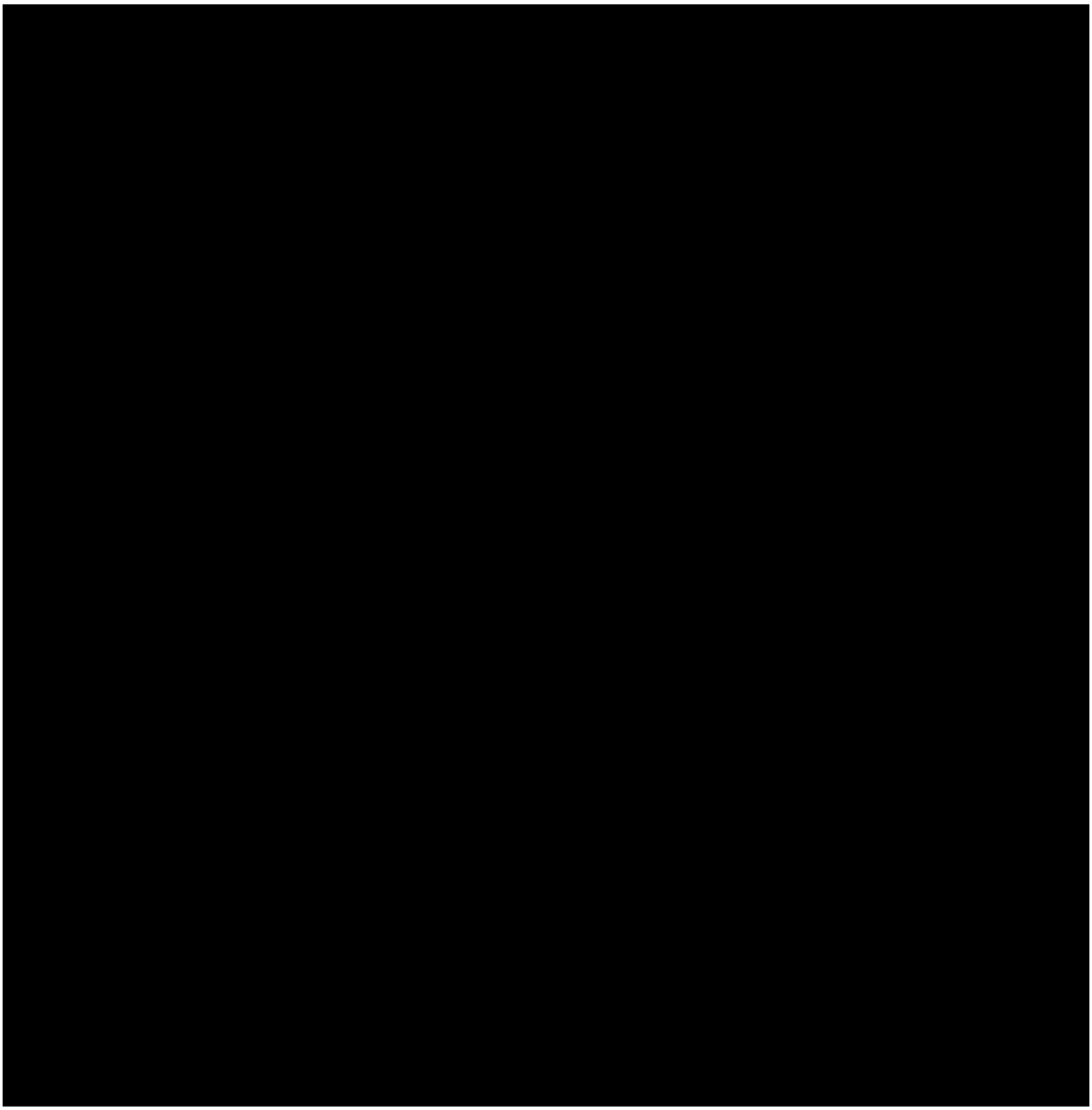
Total Stack Release: [redacted] kg/yr

Max Annual Average Air Concentration (Stack): [redacted] µg/m^3

Max 24 Hour Average Air Concentration (Stack): [redacted] µg/m^3

Exposure Units	Results (Stack)	Results (Fugitive)	ASSUMPTIONS			
			ED (years)	AT (years)	BW (kg)	Inh. Rate (m^3/hr)
Cancer						
$LADD_{pot}$ (mg/kg/day)	**2.82E-06**	**4.54E-06**	30.00	75.00	71.80	0.55
$LADC_{pot}$ (mg/m^3)	1.54E-05	2.47E-05	30.00	75.00	NA	NA

Inhalation Comments:



[redacted]